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ANNALS OF
INTERNAL MEDICINE

VOLUME 7 MARCH, 1934 NUMBER 9

# THE SIGNIFICANCE OF THE HYPERTROPHY AND HYPERPLASIA OF THE PARATHYROID GLANDS IN RICKETS AND OSTEOMALACIA *

By RUSSELL M. WILDER, M.D., GEORGE M. HIGGINS, PH.D., and CHARLES SHEARD, PH.D., *Rochester, Minnesota*

THE earliest suggestion of a correlation between the function of the parathyroid glands and rickets is to be found in a contribution of Erdheim [2] in 1906. Extirpation of the parathyroid glands of young rats led to decalcification of the dentin of the incisor teeth and to dental abnormalities resembling those found in spontaneous rickets of rats. In the normal rats, after parathyroidectomy, an increased amount of osteoid tissue developed, especially in the ribs; fractures occurred and the deposit of calcium in the calluses of the fractures was deficient. A cartilage typical of rickets was not seen, but this discrepancy was explained by retarded growth, and it was Erdheim's opinion that parathyroid deficiency leads to disturbances of ossification which are essentially the same as those of rickets.[4, 5] He had observed, in the meantime, enlargement of the parathyroid glands in cases of osteomalacia [3] of man, as well as in two cases of late rickets of human beings, and thus he arrived at the conclusion that the parathyroid glands must be inadequate at the time of onset of these conditions. The calcium-impoverishment in rickets, like that which follows parathyroidectomy, indicated, for him, a failure of parathyroid function, and the enlargement of the parathyroid glands, as observed in osteomalacia and rickets, an attempt at compensation. It should be recalled that these observations and conclusions antedated the discovery of vitamin D, and that the etiology of these skeletal diseases at that time was a matter of conjecture.

Others were quick to confirm Erdheim's finding of enlargement of parathyroid glands in osteomalacia, but his conclusions encountered some opposition for the reason that gross enlargement of these glands was not found in infantile rickets, either by himself or others. He explained it on the ground that a large majority of infants suffer from rickets, so that criteria regarding the size of perfectly normal infantile parathyroid glands were

* Read before the Central Society for Clinical Research, Chicago, Illinois, October 27, 1933.

From the Division of Medicine, Division of Experimental Medicine, and the Division of Physics and Biophysical Research, The Mayo Clinic and The Mayo Foundation.

lacking. This matter is still unsettled, but since then it has been conclusively demonstrated by Nonidez and Goodale [16] and Higgins and Sheard [10] that deprivation of vitamin D, in chickens, not only produces rickets, but is regularly accompanied by very evident hypertrophy and hyperplasia and gross enlargement of the parathyroid glands. The consistency of this is such as to suggest a direct correlation between the demand for the parathyroid product and the availability of vitamin D, a correlation which we believe to have been further elucidated by experiments to be described.

The terms "hypertrophy" and "hyperplasia" are so frequently mishandled as to make it necessary to define the usage intended. Hypertrophy is applied, by us, to an increase in the size of the individual epithelial cells of the organs in question and hyperplasia to an obvious increase in the number of these cells. Enlargement of the glands may result from either hypertrophy or hyperplasia, or from both, or from some such pathologic process as cyst formation, with or without hypertrophy, or hyperplasia.

The majority of those interested in rickets and osteomalacia have accepted Erdheim's opinion that the parathyroid enlargement of osteomalacia is an index of increased parathyroid function, but no proof for this has been submitted, and others, notably Klemperer,[13] have considered that the enlarged glands are actually depressed in function, "a fruitless attempt to compensate for calcium deficiency." It seemed to us that this question could be settled very simply. Parathyroid hormone could be administered to chicks deprived of vitamin D, and if, as supposed, the hypertrophy and hyperplasia of parathyroid glands resulting from deficiency of vitamin D is an index of increased demand for parathyroid product, the supplying of the product by injection might prevent the development of these abnormalities. Experiments of this nature might also reveal to what extent the parathyroid product would compensate for deficiency of vitamin D.

## Experiment 1 *

Six week old chicks from the same hatching of the eggs of one flock of pure bred White Leghorn hens received diets containing 2 per cent of a crude commercial cod liver oil. This had not been assayed for vitamin potency (table 1). The season was midwinter and the pens were situated

Table I

Chicken Diet for Experiment 1

| | |
|---|---|
| Yellow corn meal | 56 |
| Wheat middlings | 18 |
| Powdered buttermilk | 18 |
| Salt | 1 |
| Sand grits | 5 |
| Cod liver oil | 2 |
| Calcium by analysis | 0.45 per cent |
| Phosphorus by analysis | 0.48 per cent |

* The results of this earlier experiment were the subject of a preliminary report. Higgins, Sheard and Wilder: Proc. Staff Meet., Mayo Clinic, 1932, vii, 311–313.

behind windows of ordinary glass so that the amount of ultra-violet radiation was reduced to a minimum. Thus the cod liver oil was the only important source of vitamin D.

The birds were divided among six pens, A to F, two males and two females to a pen. The diet in pens C, D and F was supplemented with 5 per cent of bone ash which proved to be without significance. The birds in pens A and C were injected daily with 0.8 unit of parathormone (Lilly) for each 100 gm. of body weight; those in pens B and D received, in the same manner, 1.6 units for each 100 gm. of body weight. These injections were continued for six weeks. All of the birds thrived. The curves of the weight changes with and without parathormone were essentially alike. Roentgenograms gave no evidence at any time of any changes in the bones, and the values for serum calcium were normal throughout (table 2).

TABLE II

Serum Calcium and Phosphorus Values of Chicks at Close of Experiment 1

| Pen | Calcium, mg. per cent | Phosphorus, mg. per cent |
|---|---|---|
| A * | 13.27 | 5.78 |
| B * | 13.87 | 5.86 |
| C * | 13.17 | 5.76 |
| D * | 12.88 | 5.52 |
| E | 12.74 | 5.59 |
| F | 13.05 | 5.71 |

* The birds in pens A, B, C and D received daily injections of parathormone (Lilly).

However, in all the chicks in pens E and F to which no parathormone had been given, with one exception, there was some degree of abnormality in the parathyroid glands. It ranged from simple hypertrophy to frank hyperplasia. In many cases the glands were several times as large as normal and contained cysts. The abnormality was unrelated in degree to the amount of calcium in the diet. It was less intense, but otherwise entirely like that previously described by Higgins and Sheard for chicks deprived of vitamin D.

In contrast to the pathologic appearance of the parathyroid glands of the control birds, the parathyroid glands of the chicks which received parathormone were normal in appearance, both grossly and pathologically. It was concluded that the crude cod liver oil in the diet provided a relatively inadequate supply of vitamin D.* Rickets was prevented by this small amount of vitamin D, but not the hypertrophy and hyperplasia of the parathyroid glands, and, since administering parathormone medicinally had prevented alteration of the glands, it seemed reasonable to infer that the glands of the untreated chicks had been called on to deliver a larger than normal supply of hormone which in turn had resulted in their compensatory hypertrophy and hyperplasia.

* This conclusion is confirmed by the absence of alterations of the parathyroid glands in control experiment B (page 1065).

Experiment 1 had been designed with quite another objective. We were aiming at the production in chicks of the fibrous osteosis of hyperparathyroidism, such as had been obtained in rats, guinea pigs and puppies by Jaffé and his associates and by Johnson [12] and Wilder. This failed. The chick has proved highly resistant to injections of parathormone. The observation that parathormone prevented hypertrophy and hyperplasia of the parathyroid glands was accidental. It prompted our undertaking the following experiments in which chicks were more rigidly deprived of vitamin D.

## Experiment 2

A flock of 36, ten day old White Leghorn chicks from one hatching of the eggs of one flock of pure bred hens, was placed behind amber glass * and the birds were given a ration greatly deficient in vitamin D and relatively poor in calcium and phosphorus. It was essentially the same as the diet of experiment 1 (table 1) but the cod liver oil was omitted.

One group of these birds, 24 in number, was treated from the beginning with 0.8 unit of parathormone for each 100 gm. of body weight. This was injected daily, subcutaneously.

The calcium and phosphorus values of the blood serum of a few individuals of both the treated and the untreated groups are given below (table 3). No significant differences are observable in these; the value for calcium

Table III

Serum Calcium and Phosphorus Values of Chicks at Close of Experiment 2

| Calcium, mg. per cent | Phosphorus, mg. per cent |
|---|---|
| 8.47 | 6.06 |
| 6.11 | 6.12 |
| 5.91 | 6.25 |
| 6.90 * | 4.63 * |
| 5.52 * | 6.61 * |

* Values followed by an asterisk were obtained in individual birds treated with parathormone; values not so designated were obtained in individual birds of the untreated group. All the birds gave clear evidence of rickets.

is low in both groups. However, the degree of rickets in the birds treated with parathormone was somewhat less, and also the group thus treated with parathormone had gained an average of 135 gm. as compared to 108 gm. in the untreated group (table 4). The parathyroid glands in both groups revealed hypertrophy and hyperplasia but these processes were less prominent in the treated birds.

Ten of the parathyroid-treated birds from experiment 2 which had not been killed at the end of that experiment, were placed on a diet in which meat scraps replaced the dried buttermilk of the previous diet. Particles of bone in the meat scraps raised the values for calcium and phosphorus (table 5). The sand grit was also increased. In half of this flock the

* Pittsburgh glass No. 54, as used previously by Higgins and Sheard.

TABLE IV

Average Weights of Chicks in Experiment 2

| Date, 1932 | Birds receiving parathormone, 0.8 unit per 100 gm. weight, gm. | Birds receiving no parathormone, gm. |
|---|---|---|
| 6–28 | 90 | 96 |
| 7– 5 | 144 | 126 |
| 7–11 | 183 | 154 |
| 7–18 | 201 | 185 |
| 7–25 | 225 | 204 |

All birds were rigidly deprived of vitamin D. They were 10 days old 6/28/32.

TABLE V

Diet of Birds in Experiment 3

| Food | |
|---|---|
| Yellow corn meal | 58 |
| Wheat middlings | 18 |
| Meat scraps containing bone | 18 |
| Salt | 1 |
| Sand grits | 10 |
| | 105 |
| Calcium by analysis | 1.44 per cent |
| Phosphorus by analysis | 0.93 per cent |

previous treatment with parathormone was continued as before; in the other half, it was discontinued. After 11 days on this regimen all the birds were killed.

During life, no difference was apparent between the birds that continued to receive parathormone and those that had received no further treatment. The value for serum calcium remained low in both groups. Examinations of the parathyroid glands, however, revealed smaller glands in the birds that had continued on the parathormone and less evident hypertrophy and hyperplasia.

## EXPERIMENT 4

A group of 15, four week old chicks from a hatching of eggs from a flock of Brown Leghorn hens, was placed behind amber glass and given the diet recorded under experiment 3 (table 5). Six birds of this flock were treated with parathormone in a dosage of 0.8 unit daily for each 100 gm. of body weight. The remainder received no parathormone.

A significant difference was noted in the growth of these two groups, although rickets developed in both. After eight weeks (the chicks now being 12 weeks old) all the birds were killed for examination. At this time the treated birds had increased in weight an average of 297 gm. as compared to 207 gm. for the untreated birds (table 6). The parathyroid glands were hypertrophic and hyperplastic in both groups but these changes were less marked in the treated birds.

TABLE VI

Average Weights of Chicks in Experiment 4

| Date, 1932 | Birds receiving parathormone, 0.8 unit per 100 gm. weight, gm. | Birds receiving no parathormone, gm. |
|---|---|---|
| 8– 1 | 231 | 213 |
| 8– 8 | 279 | 237 |
| 8–15 | 321 | 291 |
| 8–22 | 339 | |
| 8–29 | 408 | 345 |
| 9– 5 | 432 | 360 |
| 9–12 | 456 | 360 |
| 9–19 | 504 | 360 |
| 9–26 | 528 | 420 |

All birds were rigidly deprived of vitamin D. They were 28 days old 8/1/32.

## CONTROL EXPERIMENT A

Twelve chicks, ten days old, from the same hatching as those used in experiments 2 and 3 were placed behind "vitaglass," which transmits ultra-violet light, and were fed the diet of experiment 3 (table 5). One-half of this flock received daily subcutaneous injections of parathormone in the same dosage used in experiments 2 and 3. There was no rickets and after 12 weeks, direct and microscopic examination of the bones revealed no abnormalities. The parathyroid glands of the treated birds showed some evidence of involution in the form of a fibroblastic invasion. The values for serum calcium and serum phosphorus were normal in both groups. The growth was somewhat less rapid in the birds treated with parathormone than in the birds not so treated (table 7). This result is exactly the opposite of that obtained with birds deprived of vitamin D, as in experiment 2.

TABLE VII

Average Weights of Chicks in Control Experiment A

| Date, 1932 | Birds receiving parathormone, 0.8 unit per 100 gm. weight, gm. | Birds receiving no parathormone, gm. |
|---|---|---|
| 6–28 | 90 | 90 |
| 7– 5 | 144 | 141 |
| 7–11 | 168 | 210 |
| 7–18 | 208 | 243 |
| 7–25 | 255 | 279 |
| 8– 1 | 330 | 390 |
| 8– 8 | 424 | 498 |
| 8–15 | 552 | 624 |
| 8–22 | 648 | 720 |
| 8–29 | 720 | 816 |
| 9– 5 | 780 | 816 |
| 9–12 | 780 | 900 |
| 9–19 | 780 | 1110 |
| 9–26 | 840 | 1278 |

Birds all under vitaglass, thus supplied with vitamin D. Diet same as in experiment 3. Birds were 10 days old 6/28/32.

### Control Experiment B

Twelve chicks, four weeks old, from the same hatching as those used in experiment 4, were placed behind amber glass and received the diet used in experiments 3 and 4 (table 5) but supplemented by 3 per cent of crude commercial cod liver oil. Half of this flock was given daily injections of parathormone in the same dosage used in experiment 4. No weakness of the legs was apparent. Growth was practically the same in both groups (table 8). Treatment with parathormone neither increased it, as in the

Table VIII

Average Weights of Chicks in Control Experiment B

| Date, 1932 | Birds receiving parathormone, 0.8 unit per 100 gm. weight, gm. | Birds receiving no parathormone, gm. |
|---|---|---|
| 8– 1 | 279 | 234 |
| 8– 8 | 321 | 255 |
| 8–15 | 381 | 291 |
| 8–22 | 471 | 441 |
| 8–29 | 561 | 441 |
| 9– 5 | 564 | 513 |
| 9–12 | 648 | 618 |
| 9–19 | 720 | 687 |
| 9–26 | 768 | 771 |

Birds all under amber glass receiving the diet used in experiment 4 but supplemented by 3 per cent of crude commercial cod liver oil. Birds 28 days old on 8/1/32.

case of the birds deprived of vitamin D, in experiment 4, nor decreased it as appeared in control experiment A.

After eight weeks the birds were killed for examination. The parathyroid glands of those which had received parathormone were rather markedly invaded with fibroblastic tissue suggesting functional involution. The glands of those not treated with parathormone appeared normal.

The bones of the birds treated with parathormone revealed, on microscopic examination, a slight but definite degree of lacunar resorption with replacement of cancellous structure by fibrous connective tissue. This is the first time in a large series of experiments that such evidence of fibrous osteosis has been obtained in the chick.

### Comment

The following recapitulation of the evidence now at hand will simplify its interpretation:

*Evidence for Increased Parathyroid Function in Conditions of Deficiency of Vitamin D.* 1. The parathyroid glands of chicks deprived of vitamin D are consistently enlarged (Nonidez and Goodale, Higgins and Sheard).

2. Gross enlargement is frequently associated with cyst formation, but depends primarily on an increased size of the "chief" cells, hypertrophy, due to an increased amount of the cytoplasm of these cells. This is accom-

panied by an increase in the number of cells, hyperplasia (Higgins and Sheard).

3. Enlargement, hypertrophy and hyperplasia are roughly proportional to the severity of deprivation of vitamin D, moderate in experiment 1, much more marked in experiments 2 and 4.

4. Restoring vitamin D to chicks, previously deprived of this vitamin and suffering with florid rickets, not only causes the rickets to "heal," but is followed by early regression of the accompanying parathyroid abnormality. The glands not only diminish in size but the individual cells resume their normal size.*

5. The enlargement, hypertrophy and hyperplasia of the parathyroid glands in deficiency of vitamin D is counteracted by subcutaneous injections of parathormone. In experiment 1, in which the deprivation of vitamin was insufficient in degree to provoke rickets, the hypertrophy and hyperplasia were prevented by these injections. In experiments 2, 3 and 4 in which the deprivation of vitamin was more severe, there was still some evidence of inhibition in most cases.

Other evidence for increased parathyroid function in rickets has been reported by Hamilton and Schwartz.[6] Calcium salts administered by mouth to normal rabbits increased the serum calcium to a very slight degree, but if normal rabbits were previously given injections of parathormone, the same dose of calcium usually caused death from hypercalcemia. Rachitic rabbits behaved in such experiments as the normal rabbits behaved which previously had been given injections of parathormone.

*Evidence for a Compensation Effected by an Increased Secretion of the Parathyroid Product in Deficiency of Vitamin D.* 1. The minor degree of deficiency of vitamin D, in experiment 1, provoked hypertrophy and hyperplasia of the parathyroid glands not accompanied by any of the more common skeletal lesions of rickets. It is inferred that the augmented supply of parathyroid product derived from these glands sufficed to prevent the development of rickets.

2. The more extreme degrees of the vitamin deficiency in experiments 2, 3 and 4 provoked rickets despite any compensatory action by the enlarged glands. The injection of parathormone under such circumstances diminished the degree of the rickets but did not prevent its development. The doses used were relatively large (0.8 unit per 100 gm. of body weight).

3. The growth of chicks deprived of vitamin D was favored by injections of parathormone in experiments 2 and 4, although when vitamin D was adequately supplied, as in control experiments A and B, no such growth-promoting effect was observable.

The evidence presented warrants the conclusion that the parathyroid glands are driven to increased functional activity by deficiency of vitamin D. It further reveals that increasing the supply of the hormone affords some protection against deficiency of the vitamin. It does not explain the nature

* Experiments reported elsewhere (Higgins, Sheard and Wilder [11]).

of the protection afforded but other information now at hand bears directly on this question.

It is evident, in the first place, that the hormone does not directly replace the vitamin. In itself it has no vitamin D effect. Extra hormone, whether from hyperactive glands or supplied by injection of commercial hormone, prevents the development of rickets only when the deficiency of vitamin is relatively slight. Indeed the protection afforded by the hormone is directly proportional to the amount of vitamin D available. In experiment 1, in which the diet contained 2 per cent of crude cod liver oil, the protection afforded by the hormone was complete. In experiments 2, 3 and 4, with very rigid deficiency of vitamin D, the protection was unsatisfactory, but still in evidence. Presumably if the vitamin could be completely excluded no amount of hormone would protect at all.*

A second possibility, namely, that the hormone increases vitamin D effects by activating the vitamin, is unlikely. If it were true one would expect the potency of the commercial hormone to be the same, irrespective of the species of animal into which it is injected. It is not. Parathormone in doses of 1 unit per kilogram of body weight is noticeably active in man, whereas 20 times this dose given to normal chicks has little or no effect.

An explanation that seems to fit is the following: The hormone is not the vitamin, nor does it act like the vitamin, nor does it sensitize or activate the vitamin; its action is on the tissues of the organism which it sensitizes or conditions, so that the tissues can function normally with less vitamin than otherwise would be necessary. Support for this hypothesis is found in the following observations:

The discovery of Erdheim that parathyroidectomy is followed by decalcification of the dentin of the teeth of rats and failure to deposit calcium in the calluses of fractures, has been mentioned in the introduction. His interpretation of this observation, restated in the light of present day knowledge of the etiology of rickets, would be that a normally adequate supply of vitamin D becomes inadequate when the parathyroid hormone is removed. Hess and Lewis [7] and later Hess, Weinstock and Rivkin [8, 9] reported the following: viosterol promptly raised the value for serum calcium in monkeys and dogs in which latent tetany was induced by deprivation of calcium, but after the parathyroid glands had been removed the value for serum calcium fell again and was then unaffected by doses of viosterol 40 times that which is prescribed for infants of equivalent weight. However, much larger doses of viosterol, in later experiments of Hess and his associates and according to Jones, Rapoport and Hughes † and Demole and Christ,[1] are effective even after parathyroidectomy. Kozelka [14, 15] has made a similar comment.

* Young chicks store a certain small amount of vitamin D, obtained presumably from the yolk of eggs from which they hatch. Complete deprivation of vitamin D is thus excluded as a possibility in experiments of this nature.

† It is an open question in all experiments of this kind, whether all existing parathyroid tissue has been resected. Accessory parathyroids are extremely difficult to uncover. It may be that in the absence of any parathyroid tissue whatsoever the organism would be quite insensitive to vitamin D.

Thyroparathyroidectomized dogs could be maintained free from tetany by giving vitamin D, but the doses required were several times as large as are normally required. In parturient animals several thousand rat units were used daily. Doses of this magnitude given to normal animals produce evidences of hypervitaminosis, as described by Hess and others. An abnormally high tolerance for vitamin D in parathyropriva is also apparent from the observations of Seeds and Reed.[17]

The other side of the picture is presented in observations of Johnson, working under the direction of one of us (Wilder), on the production in rats and puppies of the bony lesions of hyperparathyroidism. Johnson injected rats with parathormone in doses of from 2 to 20 units daily and uniformly produced the typical picture of parathyroid osteosis. Litter mates of these animals, receiving identical doses of parathormone, were given daily doses of 10 to 15 small drops of viosterol, representing not more than from 60 to 90 Steenbock units of vitamin D. In normal rats this dose of vitamin D was without noticeable toxic effect, but given with the parathormone it produced intense metastatic calcification of the kidneys. The conclusion to be drawn from these data must be that the sensitivity of an animal to vitamin D is decreased in parathyroid insufficiency and increased in conditions of parathyroid excess, which means, as stated in the hypothesis, that the hormone sensitizes the tissues of the organism to the action of the vitamin.

It may be asked whether the stimulus to the parathyroid glands in conditions of deficiency of vitamin D is the lack of vitamin, per se, or the resulting hypocalcemia. In experiment 1 the parathyroid glands became hypertrophic and hyperplastic in the presence of a normal value for serum calcium, which seems to point to a direct effect on the glands.

## Conclusions

Experiments with chicks reveal that deprivation of vitamin D, insufficient in degree to cause rickets, will produce hypertrophy and hyperplasia of the parathyroid glands; that the parenteral administration of parathormone in such minor degrees of deprivation of vitamin D prevents this hypertrophy and hyperplasia, but that when the deprivation of vitamin D is extreme, so that rickets is clearly in evidence, administering parathormone may restrict but will not prevent the hypertrophy and hyperplasia of the glands.

It appears from this and other evidence cited that the hypertrophy and hyperplasia of the parathyroid glands of chicks, under conditions of deficiency of vitamin D, depend on their accelerated functional activity.

Other observations are interpreted to mean that the supply of parathyroid hormone determines the sensitivity of the organism to the action of vitamin D. A diminished supply of the hormone, as after parathyroidectomy, diminishes the ability of the organism to function normally with restricted amounts of vitamin D; an augmented supply conditions the tissues of the organism so that the effects of the vitamin are more intense, and so that

amounts of the vitamin which otherwise would not prevent rickets, do prevent rickets.

By virtue of the capacity of the parathyroid glands to accelerate the rate of supply of their product, and owing to the resulting conditioning of the tissue (increased sensitivity to vitamin D), the organism is enabled to withstand periods of relative deficiency of vitamin D which otherwise would produce rickets or osteomalacia. This compensatory mechanism is adequate to protect against relative degrees of deficiency of vitamin D; it is inadequate, as would be expected, when deficiency of vitamin D is extreme.

We are indebted to the Eli Lilly Company for supplying the parathormone used in this investigation.

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# CHRONIC PERICARDIAL EFFUSION IN MYXEDEMA: REPORT OF CASE *

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The cardiac disturbances associated with hyperthyroidism have long been recognized, as shown by the abundance of literature which has accumulated on the subject. Equally striking is the comparative dearth of publications dealing with the cardiac disturbances associated with hypothyroidism. In fact, nothing on this subject is to be found in the literature until 1918, when Zondek [1] described under the term "Myxedema Heart" certain cardiac signs and symptoms observed in some myxedematous patients, namely: enlargement of the heart, feeble heart action, slow heart beat, normal blood pressure, and low amplitude of the auricular P- and the final ventricular T-waves in the electrocardiogram. Since Zondek's original article was published, other articles dealing with the heart in myxedema have appeared in the literature at irregular intervals. The characteristic appearance of the heart as described by Zondek has been attributed to a number of conditions, namely: diffuse dilatation of the heart; edema of the heart and the tissues surrounding the heart; cardiovascular disturbances not dependent upon myxedema; and possibly to effusion into the pericardium. Since it has been proved that pleural and peritoneal effusions occur in some cases of myxedema, it seems logical to assume that a similar collection of fluid may likewise occur in the pericardium.

Fahr [2] believes that heart failure is a prominent feature in pronounced cases of myxedema. He claims that the shape of the heart in myxedema is very characteristic and differs very materially from that found in well known types of cardiac disease. He states that in defects of the mitral valve, there is bulging of the conus arteriosus and the pulmonary artery in the second and third interspaces, with displacement of the right auricular border to the right. In myxedema heart, this bulging does not occur. In lesions of the aortic valve and in hypertension, cardiac dilatation involves the left ventricle exclusively or, in the later stages, to a greater extent than the right. This again differs from myxedema heart in which all chambers dilate equally. Fahr further states that in a pericardial effusion of moderate degree, the heart shadow may resemble that seen in myxedema heart. In massive effusion, however, the base of the heart is much broader than in myxedema heart. He stresses the point brought out by Zondek, that when the myxedema heart is examined fluoroscopically, the heart borders move very sluggishly. This he attributes to marked dilatation; and he does not believe that any conclusion as to the strength of contraction can be drawn from observation of the heart borders.

Means, White and Krantz [3] made an analysis of the cases of myxedema studied in the Thyroid Clinic of the Massachusetts General Hospital, cover-

* Read before The Baltimore City Medical Society, March 3, 1933.

ing a period of 12 years—48 in all. They found one case only in which there was definite cardiac enlargement, which subsided under thyroid therapy. The initial enlargement in this case was not as pronounced as in Fahr's cases. From their study, they concluded that myxedema heart, in the sense of Zondek and Fahr, is far from common. They are not, however, willing to join those who feel that it does not exist. They further state that the evidence produced by Zondek and Fahr of marked cardiac dilatation which disappears quickly under thyroid medication, is incontrovertible; and their case, in a less striking way, is one in point. They believe the type of disability described by Zondek and Fahr must be functional in character, in that it responds so well to thyroid therapy. They have, however, no explanation as to why myxedema heart is not more frequently found in cases of myxedema.

Means,[4] in a more recent article, suggests that the cardiac enlargement found in some cases of myxedema may possibly be due either to hypertrophy, pericardial effusion, edema or dilatation. " Because of the rapid shrinkage, hypertrophy is unlikely (unless of course, some independent cause for it, like hypertension, is present). By the same token, dilatation seems likely. At least, it is easy to believe that shrinkage could be due to the rapid improvement in tone under the action of thyroid. Pericardial effusion is possible, but the x-ray appearance is against it. Some edema of the heart muscle may play a part. It was noted at autopsy in our cases, and it is easy to conceive of its rapid disappearance under thyroid."

Lerman, Clark and Means,[5] in a still more recent article, arrived at the following conclusions: " Myxedema heart in the sense of cardiac enlargement which undergoes shrinkage on thyroid medication is common. . . . The heart changes are to be regarded as a part of myxedema—not as a separate cardiac entity. . . . The change in the heart with thyroid treatment is probably due to increased muscle tonus and loss of interstitial edema. In an occasional case the loss of pericardial fluid may account for this change."

Willius and Haines[6] made a careful study of 162 cases of high grade myxedema, with special reference to the cardiovascular system. As to age incidence, they found the disease was most frequent in the fourth, fifth, and sixth decades, in which 32, 52 and 38 cases, respectively, were recorded; there were 128 females and 34 males. In 148, or 91 per cent, there were no subjective symptoms or objective signs indicative of cardiovascular disease. Eleven cases, or 7 per cent, presented definite evidence of organic cardiovascular disease, which was only in one instance influenced by the disappearance of myxedematous symptoms under thyroid therapy. Their conclusions were as follows: " In 162 cases of high grade myxedema studied, none of heart failure and none of organic cardiovascular disease were found that could be justly attributed to the myxedema. There were numerous electrocardiographic abnormalities which disappeared under thyroid medi-

cation. The data presented do not justify the establishment of a cardiac syndrome characteristic of myxedema."

Ayman, Rosenblum and Falcon-Lesses [7] analyzed 22 cases of myxedema heart previously reported in the literature, and report two additional cases that have come under their observation. They mention as probable causes of myxedema heart: cardiac dilatation secondary to a flabby heart muscle; myxedematous conditions of the heart itself or the tissue about the heart; and the existence of pericardial fluid.

Evans [8] reports a case of myxedema with ascites and atony of the urinary bladder. He mentions six cases of ascites associated with myxedema previously reported in the literature. Five of these were reported by Fournier; in two of the five, there was also pleural effusion. The sixth was reported by Marsh. In this case three gallons of fluid were removed by abdominal paracentesis, following which the fluid gradually returned. It finally disappeared under thyroid therapy. In his summary he states: "A case is reported of well advanced myxedema presenting the unusual features of atony of the bladder, myxedema heart, and free fluid in the abdominal and pleural spaces. The fluid in the abdomen was found to have an unusually high protein content. It is believed that the atony of the bladder was a result of thyroid insufficiency and that the free fluid represented true myxedema fluid and not a manifestation of cardiac failure."

In a personal communication Christian [9] states: "So far as I know, there are no observations in the literature in regard to pericardial effusion in myxedema. From time to time, people have expressed the idea that so-called myxedema heart was pericardial effusion and not an involvement of the myocardium, but I think no one has proved this. . . . The rapid decrease in the size of the heart following thyroid administration has also made this explanation of pericardial effusion probable. However, the only real proof will be the actual tapping of the pericardium with removal of the fluid. I have myself observed and proved by tapping, both peritoneal and pleural, accumulations of fluid in myxedema, and then have seen them disappear with thyroid extract. Consequently, I am entirely expectant of seeing the same thing happen with the pericardium."

Gordon,[10] in a report on "Some Clinical Aspects of Hypothyroidism," calls attention to the occasional similarity of its clinical manifestations to those of pernicious anemia, chronic nephritis, migraine, and pericarditis with effusion. In his paper, he describes one case of myxedema with pericardial effusion occurring in a man of 68, whose complaints were shortness of breath and swelling of the face and lower extremities. On physical examination the cardiac dullness measured 24 centimeters laterally; the heart sounds were almost inaudible; roentgen-ray examination confirmed the presence of pericardial effusion. The basal metabolic rate was minus 42. On two occasions, the pericardium was tapped and 1500 c.c. of clear amber fluid were removed. Inoculation of a guinea pig with this fluid yielded no evidence of tuberculosis. On properly graduated doses of

thyroid extract the basal metabolic rate returned to normal, and the pericardial effusion disappeared.

In view of the fact that so few cases of effusion into the serous cavities of the body in myxedema have been reported and since, as far as I am able to determine, in only one of these did the effusion occur in the pericardial sac, I herewith submit the following report:

## Case History

A. W. H., male, aged 39, referred by Dr. George W. Murgatroyd, entered the Maryland General Hospital on March 23, 1931. His family history was unimportant. His past history was negative with the exception of an illness at the age of six, which was possibly rheumatic fever. His present illness began in 1925, when he was 33

Fig. 1. Chest film on admission before pericardium was tapped.

years of age, with a feeling of exhaustion. He continued to work until March 1, 1927. One week later, he entered St. Agnes' Hospital. An abstract of the St. Agnes' Hospital records is herewith presented:

*Chief Complaint:* Marked weakness associated with cough and shortness of breath. Physical examination: pale, anemic looking young man. Skin very dry and

scaly; hair thick and dry; eyelids edematous; thyroid not palpable. Cardiac dullness increased to the left to the mid-axillary line; and likewise definitely increased to the right, with obliteration of the cardio-hepatic angle. The increase in the area of cardiac dullness found on physical examination was confirmed by roentgen-ray study. No murmurs were heard and there was no arrhythmia. The blood pressure was 110 systolic and 70 diastolic. The lungs showed moderate dullness at both bases posteriorly. The abdomen was soft, and the liver enlarged; its lower border was three fingers' breadth below the costal margin, somewhat firmer than normal, the surface smooth and regular. There was slight edema of the extremities. The reflexes were normal.

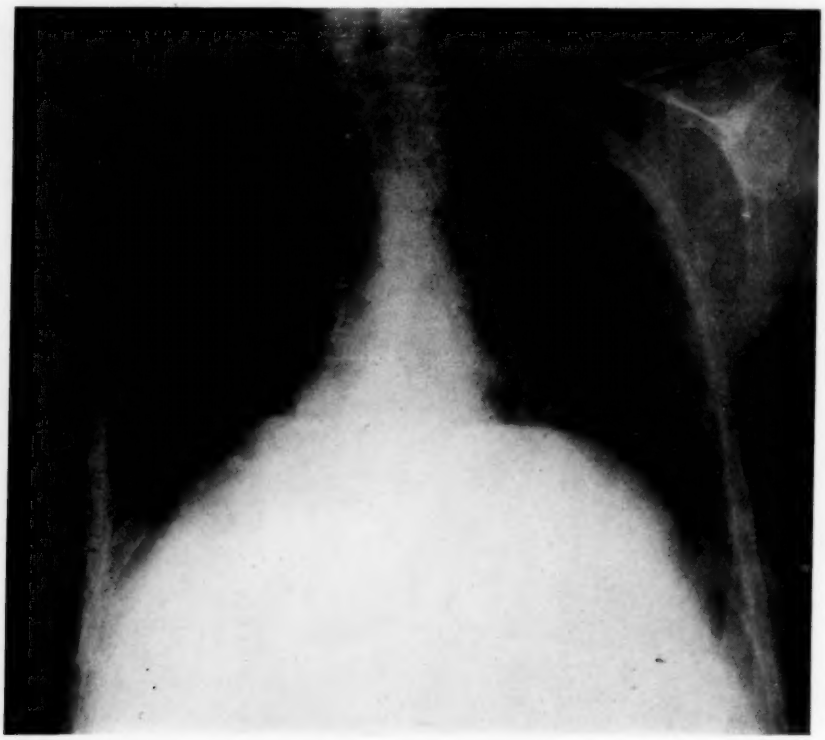

FIG. 2. Chest film taken immediately after withdrawing 450 c.c. of fluid from pericardium.

The records show the following laboratory studies: Blood Wassermann negative. Hemoglobin 70 per cent; erythrocytes 4,500,000; leukocytes 10,300; normal differential count. Van den Bergh test: direct and indirect negative. Icterus index 5. Stomach analysis (test meal): free hydrochloric acid 10 degrees; total acidity 19. Urine: specific gravity 1.020; tests for sugar and albumin negative; microscopic examination negative. Renal function test (intravenous phenolsulphonphthalein): first half hour 15 per cent; second half hour 8 per cent; total 23 per cent.

A diagnosis of chronic pericarditis with effusion was made. The pericardium was tapped and 1400 c.c. of a clear, straw colored fluid were removed. The specific gravity was 1.019. The patient remained in St. Agnes' Hospital for four weeks and was discharged very much improved. He returned to his trade, electrotyping, and worked for three months in the early summer of 1927. During this time there was

a gradual return of symptoms, and he was again compelled to give up his position. From the time he gave up his position in August 1927 until he entered the Maryland General Hospital in March 1931 (nearly four years), he remained a semi-invalid and unable to work. When he entered the Maryland General Hospital, he presented a typical picture of myxedema. His chief complaints were shortness of breath, pronounced weakness, swelling of the extremities, and great sensitiveness to cold. He was mentally very sluggish and responded to questions slowly. The least effort seemed completely to exhaust him. He was unable to lie down in comfort on account of shortness of breath. There was marked puffiness of the eyelids and face. There

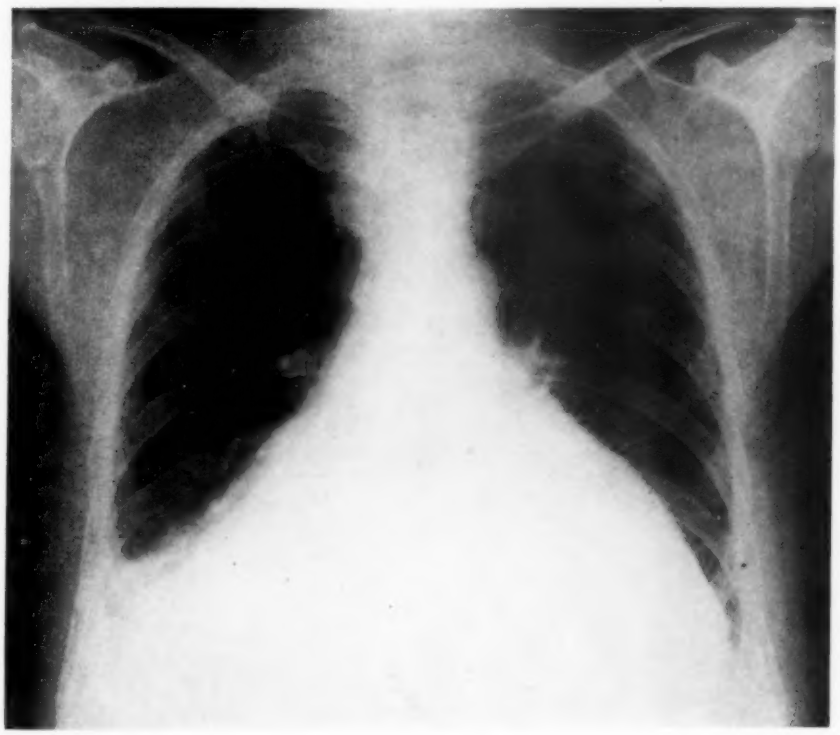

FIG. 3. X-ray film taken immediately after removal of 800 c.c. of fluid from pericardium, 14 days following first tapping.

was slight pitting edema of the lower extremities. His skin was very dry; it was especially scaly on the arms and legs, and apparently somewhat thickened everywhere. The hair was extremely dry, very coarse and thick. There was no loss of hair on any portion of the body, except on the legs below the knees. His tongue was coated and very dry. The area of cardiac dullness was markedly increased, with a transverse measurement of 24 centimeters; the cardio-hepatic angle was obliterated. The physical signs of enormous increase in the area of cardiac dullness were confirmed by fluoroscopy and roentgen-ray films. In addition to confirming these physical findings, the fluoroscopic study also showed complete absence of pulsation in the cardiac shadow. The apex beat was not visible; it was barely possible to hear the heart sounds. The pulse rate was 70 per minute and regular. The blood pressure was 120 systolic and 70 diastolic. No sclerosis of the peripheral vessels was apparent. The

lungs showed a few moist râles at both bases posteriorly. There was no shifting abdominal dullness. The liver was enlarged; its lower border was three fingers' breadth below the costal margin, somewhat firmer than normal, and not sensitive to pressure. There was slight edema of the extremities. The deep reflexes gave responses within normal limits.

*Special Studies:* Blood Wassermann negative. Hemoglobin 75 per cent; erythrocytes 3,750,000; leukocytes 7,100; normal differential count. Blood urea 32.4 milli-

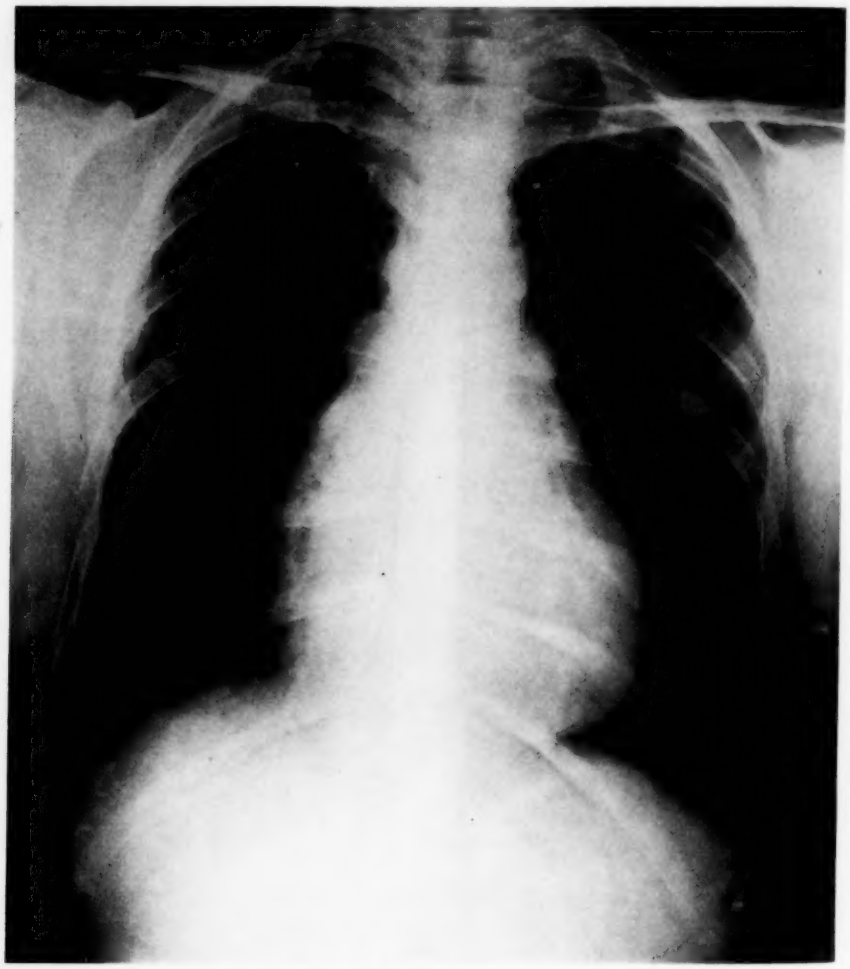

FIG. 4. X-ray film, three months after patient began taking thyroid extract.

grams per 100 c.c. blood. Stomach analysis (test meal): free hydrochloric acid 8 degrees; total acidity 22 degrees. Urine: specific gravity 1.010; albumin, trace; sugar negative; microscopic examination negative. The electrocardiogram showed the absence of T-waves and low amplitude of the QRS complexes. The basal metabolic rate was minus 45. A diagnosis of myxedema with chronic pericardial effusion was made. The pericardium was tapped and 425 c.c. of clear, straw colored fluid removed. Two weeks later the pericardium was again tapped, and an additional 800

c.c. of fluid removed. Even though 800 c.c. of fluid were removed, a large quantity still remained, as evidenced by roentgen-ray films taken immediately after the pericardium had been tapped. The fluid contained no blood and formed no clots; its specific gravity was 1.022. The Rivalta test was positive; protein 45 grams per liter. Smears: polynuclear cells 50 per cent, lymphocytes 12 per cent, endothelial cells 38 per cent. No organisms were found. Stained smears showed no tubercle bacilli; culture on blood agar remained sterile; guinea pig inoculation proved negative for tuberculosis.

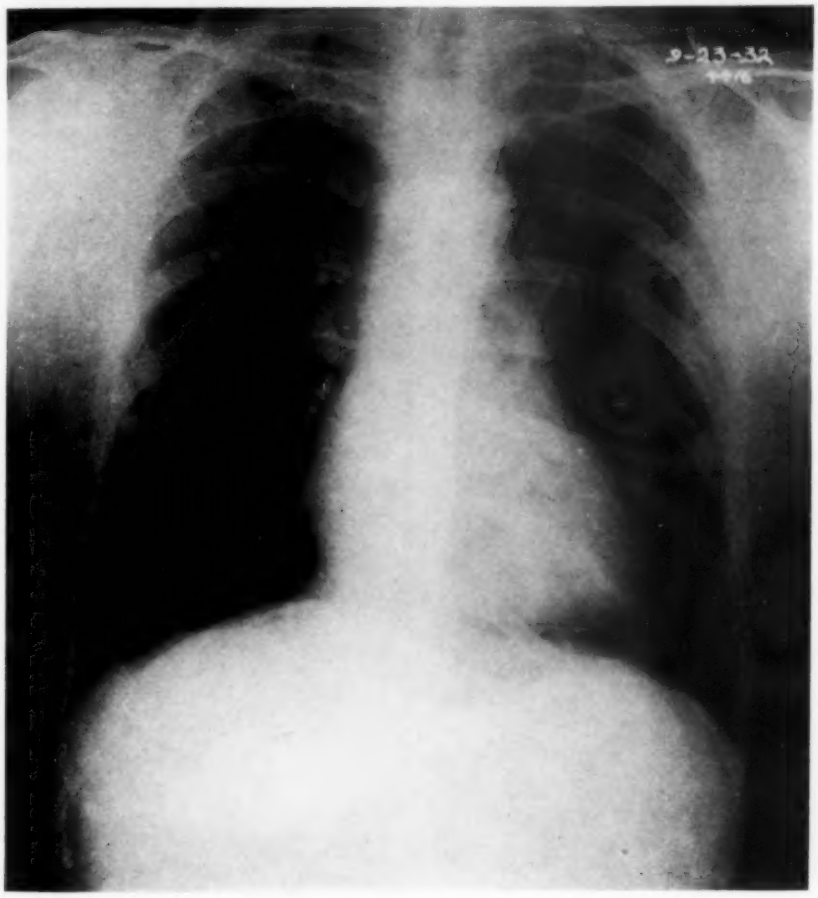

FIG. 5. X-ray film, 17 months after beginning of thyroid extract.

It is interesting to note the striking resemblance that exists between the clinical history, physical examination and the laboratory studies made in St. Agnes' Hospital and those made in the Maryland General Hospital four years later. When this is borne in mind, I think one is justified in drawing the following conclusions: (1) that the large pericardial effusion found in St. Agnes' Hospital was not due, as thought, to chronic pericarditis but to myxedema; (2) that the patient had been suffering from myxedema from the onset of his symptoms, which were first noticed six years before thyroid therapy was instituted.

The initial dose of thyroid extract was small, ¼ grain three times a day. The dose was gradually increased until at the end of three months, the patient was getting ¾ grain three times a day. This amount of thyroid brought the basal metabolic rate up from a minus 45 to a minus 10. With this rise in metabolic rate, the pericardial effusion entirely disappeared as shown by physical examination and roentgen-ray study. There was marked improvement in the patient's general condition. His mental condition returned to normal, and he became interested in life for the first time in

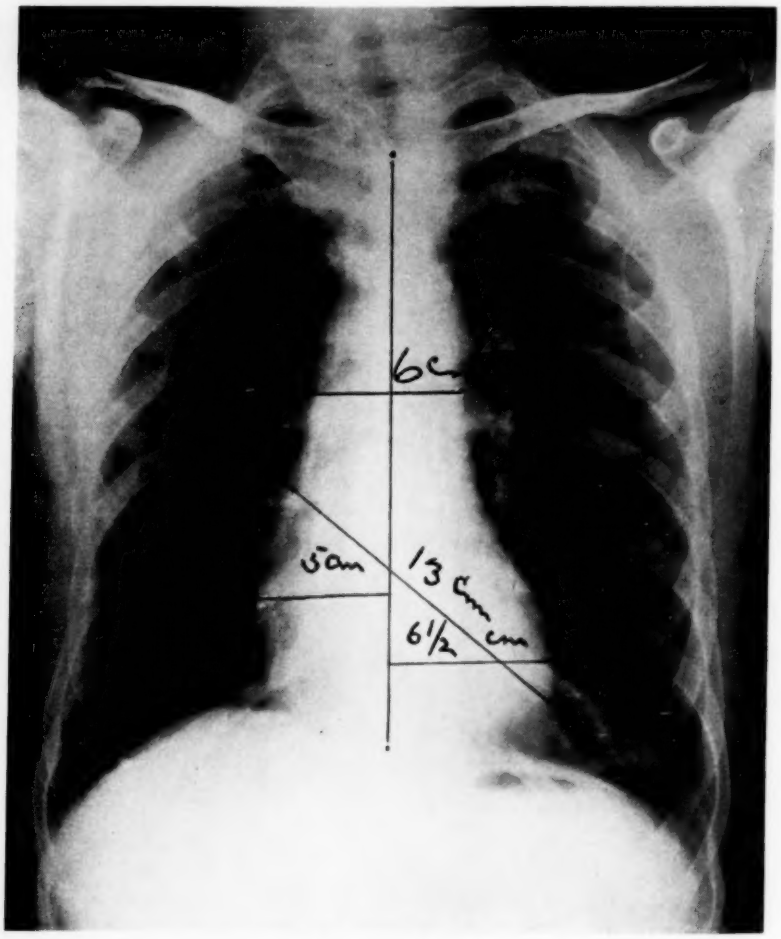


FIG. 6. Teleroentgenogram, 26 months after beginning thyroid therapy.

more than four years. The skin was moist. The edema of the face and extremities entirely disappeared and the subcutaneous thickening noticed over the entire body likewise disappeared. The electrocardiographic tracing returned to normal. The muscular weakness was very much improved. There was no attempt made to give sufficient amount of thyroid to bring the basal metabolic rate up to an absolute normal, as it seemed better judgment in this particular case to keep the metabolic rate around a minus 10; this has been done. Basal metabolic studies have been made every six months. The amount of thyroid extract required to keep the metabolic rate around a minus 10 has remained constant,—2½ grains per day for the past 18 months.

In addition to the basal metabolic determinations made at regular intervals, there have been frequent roentgen-ray studies of the heart. The heart has remained normal in size. Since the fluid disappeared from the pericardium there has been no evidence of its return. Only once since thyroid treatment was begun has it been discontinued. This was done at the suggestion of Dr. William F. Rienhoff in an effort to determine whether or not there was any change in the calcium content of the blood in chronic pericardial effusion in myxedema. The first calcium determination was made while the patient was still taking thyroid extract; this showed 10.5 milligrams of calcium per 100 c.c. blood. Thyroid therapy was discontinued for 16 days, when a second calcium determination was made; this showed 10 milligrams per 100 c.c. blood. These two determinations approximate each other so closely that it seems apparent that the stopping of the thyroid did not influence the calcium content of the blood. There was, however, a drop of 22 per cent in the basal metabolic rate in the 16 day period during which the thyroid therapy was discontinued. It is now two and a half years since thyroid therapy was instituted. Throughout this time thyroid extract has been given continuously, except for the short intermission while the blood calcium determinations were being made. No other medication has been given. While the patient's physical condition has not improved sufficiently to enable him to return to his occupation of electrotyping, he has been able, however, to do less strenuous work and has been holding a responsible office position for the past four months. He looks and feels quite well.

## Summary

A case of chronic pericardial effusion occurring in myxedema is presented. The pericardial effusion was rapidly absorbed when sufficient thyroid was given to bring the metabolic rate up to the accepted low normal. It seems apparent therefore, that chronic pericardial effusion does occur in some cases of myxedema, although the etiological relationship of the myxedema to the pericardial effusion is not clearly understood.

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# THE EFFECT OF CALCIUM ON THE STORAGE OF COLLOID IN THE THYROID GLAND *

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FOR some time iodine has been emphasized as the most important factor in thyroid function. Iodine, however, is only one factor. Calcium is another element necessary to proper thyroid function. Various aspects of the problem have been discussed by Berry,[1] Hellwig,[2] Kottman,[3] Abelin,[4] and Juanita Thompson.[5] As the latter has stated, both calcium and iodine exert important influences on the thyroid, the normal function of which seems to depend on a proper relation between these two elements. Calcium in limestone areas has been stressed as an important factor in the causation of goiter, through a water supply rich in this element. More recently Hellwig has demonstrated that excess of calcium in the presence of iodine deficiency causes hyperplastic changes in the thyroid. The results of his investigations suggest again that normal thyroid function may depend on the conjoint action of calcium and iodine. The purpose of my study is to determine what influence calcium exerts in the storage of colloid in the thyroid; particularly in the presence of thyroglobulin as well as of an excess of iodine in the water supply. The investigation was begun as a result of an interesting clinical experience in which the administration of calcium exerted a definite curative effect in acute hyperthyroidism.[6] This raised the question: What effect has calcium on the function and structure of the thyroid gland which gives it therapeutic properties in clinical hyperthyroidism?

## EXPERIMENTS

Thirty-six young white rats, 250 to 300 grams in average weight, were separated into six groups, which were kept separate in clean wire cages and were all fed a liberal general diet. Group 1 received distilled water for drinking and daily injections of 0.5 c.c. of a 2 per cent hog thyroglobulin. Group 2 was given 5 per cent calcium lactate water for drinking, and daily injections of 0.5 c.c. of a 2 per cent solution of thyroglobulin. Group 3 received distilled water for drinking, daily injections of thyroglobulin, and a daily subcutaneous injection of 1 c.c. of a 10 per cent solution of calcium gluconate. Series 1 to 3 were started on April 27, 1932 and were terminated by chloroforming on May 16, 1933. The thyroids were immediately dissected out, measured, and fixed in 10 per cent formalin. Group 4 was given 1 per cent potassium iodide in distilled water for drinking and no calcium. Group 5 received 1 per cent potassium iodide in distilled water for drinking, and daily injections of 1 c.c. of a 10 per cent solution of calcium gluconate. Groups 4 and 5 were begun on May 20, 1933 and chloroformed on June 20,

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1933. In group 4, two rats died of intercurrent infection. These were rejected. A series of six rats on the general laboratory diet and tap water served as controls. The thyroid tissues were imbedded in celloidin and sections 10 to 15 microns thick were stained with hematoxylin and eosin. Thick sections were chosen because they give a better concept of the shape and size of the follicles. In order to render the results as objective as possible, measurements of the follicles were made with an ocular micrometer. In each animal the diameters of 25 of the largest follicles were measured in scattered sections of the series and the average follicular diameter computed. As a check on the accuracy of the measurements, 100 additional follicles were counted in scattered sections of each rat series and the results tabulated. (See tables 1 and 2.) Thus in each series 250 follicles were measured. Since peripheral follicles are often larger than internal ones, half of the measurements were taken in the center of a section. In this manner a certain estimate could be obtained as to the average size of the thyroid follicle which was used as an index of colloid storage.

## Results

The results of the gross thyroid measurements and follicular index are recorded in tables 1 and 2. The normal average follicular diameter was 214 microns. This is not presented as an absolute value: the variability of the structure of the thyroid gland under diverse conditions is well known. However, under the given conditions the index may serve as a measure for comparison. In the normal resting glands, the colloid was thin, and stained faintly with eosin. In the other groups the colloid seemed dense and was markedly eosinophilic. The rats receiving thyroglobulin and no calcium showed a slight increase of colloid storage as compared with the normal; 228 microns compared to 214 microns (6 per cent). The group receiving an excess of calcium lactate in the drinking water presented the greatest storage of colloid, 49 per cent above normal. The calcium gluconate group also showed a definite increase in colloid storage, 33 per cent above normal, as compared with a 6 per cent increase with thyroglobulin alone. This appears to demonstrate that calcium increases the storage of colloid in the presence of an experimental excess of thyroglobulin. This fact may explain the therapeutic action of calcium in clinical hyperthyroidism. The storage of colloid in the presence of excessive amounts of iodine is illustrated by series 4 and 5. With no calcium, 1 per cent potassium iodide caused an apparent 10 per cent increase of colloid storage as compared to the normal. However, with the administration of calcium gluconate in the presence of an excess of iodine this increase reached 38 per cent. In group 3, rat 5 had a rather low follicular index (141 microns) and epithelial hyperplasia. This was associated with a suppuration in the trachea. The same applies to rat 2 in group 4, and rat 4 in group 5. Nevertheless the rats which received calcium showed greater colloid storage even in the presence of

TABLE I

| Rat Series | *Group 1* Distilled $H_2O$ Thyroglobulin | | *Group 2* Calcium Lactate Thyroglobulin | | *Group 3* Calcium Gluconate Thyroglobulin | | *Group 4* 1% KI Water No Calcium | | *Group 5* 1% KI Water Calcium Gluconate | | *Group 6* Normal Diet Control Series | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Diameter of Follicles, Microns | Size of Thyroid, Millimeters | Diameter of Follicles, Microns | Size of Thyroid, Millimeters | Diameter of Follicles, Microns | Size of Thyroid, Millimeters | Diameter of Follicles, Microns | Size of Thyroid, Millimeters | Diameter of Follicles, Microns | Size of Thyroid, Millimeters | Diameter of Follicles, Microns | Size of Thyroid, Millimeters |
| 1 | 200 | R.5×2×1<br>L.5×2×1 | 274 | R.5×2×1<br>L.5×2×1 | 340 | R.5×2×1<br>L.5×2×1 | 333 | R.6×3×2<br>L.6×3×2 | 311 | R.5×2×1<br>L.5×2×1 | 174 | R.6×3×1<br>L.6×2.5×1 |
| 2 | 251 | R.6×2×1<br>L.6×2×1 | 333 | R.5×2×1<br>L.5×2×1 | 290 | R.6×2×2<br>L.6×2×2 | 189* | R.7×3×1<br>L.7×3×1 | 332 | R 6×2×1<br>L.6×2×1 | 242 | R.5×2×1<br>L.5×2×1 |
| 3 | 250 | R.5×2×1<br>L.5×2.5×1 | 411 | R.5×2×1<br>L.5×2×1 | 343 | R.6×2×1.5<br>L.6×2×2 | 254 | R.6×2.5×1<br>L.6×2.5×1 | 349 | R.5×2.5×1<br>L.5×2.5×1 | 244 | R.6×2×1.5<br>L.6×2×1.5 |
| 4 | 248 | R.4×2×1<br>L.4×2×1 | 393 | R.6×2×1<br>L.6×2×1 | 298 | R.6×2×1<br>L.6×2×1 | 192 | R.8×3×2<br>L.8×3×2 | 208* | R.5×2×1<br>L.5×2.5×1 | 224 | R.5×2×2<br>L.5×2×2 |
| 5 | 238 | R.5×2×1<br>L.5×2×1 | 292 | R.5×2×2<br>L.5×2×2 | 141* | R.6×2×1<br>L.6×2×1 | Died<br>Rejected | R.7×3×1<br>L.7×3×1 | 308 | R.6×2×1<br>L.6×2×1 | 213 | R.6×2×2<br>L.6×2×2 |
| 6 | 173 | R.5×2×1<br>L.5×2×1 | 276 | R.5×2×1<br>L.5×2×1 | 379 | R.6×2×1<br>L.6×2×1 | Died<br>Rejected | R.6×2×1<br>L.6×2×1 | 329 | R.6×2×1<br>L.6×2×1 | 201 | R.6×2×1<br>L.6×2×1 |
| Average Diameter | 226 | | 329 | | 297 | | 242 | | 306 | | 216 | |

* Respiratory Infection; Suppuration in Trachea.

TABLE II

(100 Follicles in Each Series)

| *Group 1* Distilled $H_2O$-Thyroglobulin | *Group 2* Calcium Lactate-Thyroglobulin | *Group 3* Calcium Gluconate-Thyroglobulin | *Group 4* 1% KI Water No Calcium | *Group 5* 1% KI Water Calcium Gluconate | *Group 6* Normal Diet Control-Series |
|---|---|---|---|---|---|
| Diameter of Follicles, Microns | Diameter of Follicles, Microns | Diameter of Follicles, Microns | Diameter of Follicles, Microns | Diameter of Follicles, Microns | Diameter of Follicles, Microns |
| 230 | 309 | 274 | 230 | 287 | 213 |
| Average Measurement for 250 Follicles | | | | | |
| 218 | 319 | 285 | 236 | 296 | 214 |

infection. Gross measurements indicated abnormal size of follicles (colloid goiter) in rats 2, 4, and 5 in the group receiving 1 per cent potassium iodide water and no calcium. All the other animals presented practically normal measurements of the total thyroid gland (5 by 2 by 1 to 6 by 2.5 by 1 mm.). The gross appearance of the cut surface varied. The gland might appear pink with much colloid, or hyperemic and seemingly poor in colloid.

## SUMMARY

1. Calcium either by mouth or hypodermically increases the amount of colloid in the thyroid gland in the rat in the presence of excess of thyroglobulin and iodine.

2. Intercurrent respiratory infection may cause a decrease of colloid storage and of hyperplasia. Even in these animals calcium increased the storage of colloid.

3. The therapeutic action of calcium in hyperthyroidism may be due to this property of increasing colloid storage in the presence of an excess of thyroglobulin.

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# NOMENCLATURE OF THE DISORDERS OF INSULIN SECRETION: DIABETES MELLITUS, HYPERINSULINISM AND DYSINSULINISM *

## AN ANALYTICAL REVIEW OF DATA RELEVANT TO THE CLASSIFICATION AND TERMINOLOGY OF THE SECRETORY DISORDERS OF THE ISLANDS OF LANGERHANS OF THE PANCREAS

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THE classification and nomenclature of the secretory disorders of the islands of Langerhans of the pancreas is of importance, as it is in all diseases. According to the recently compiled book, " A Standard Classified Nomenclature of Disease," [1] which has been adopted by the leading hospitals in America, the ideal name for a disease should identify it with the organ involved (topographic), and with the pathologic and physiologic changes that occur in the glands, or other tissues, which cause the phenomena observed in the condition (etiologic). In the classification and nomenclature of the secretory disorders of the pituitary, thyroid and adrenal glands, the topographic and etiologic factors have been considered; thus it seems logical that the same method of nomenclature should be adopted in the terminology of the disorders of the internal secretion of the pancreas.

Rowe [2] in his recent book on " The Differential Diagnosis of Endocrine Disorders," discussing the terminology of the secretory disorders of the endocrine gland, says:

> The term hypofunction is applied to that condition in which the clinical and laboratory findings indicate a lowered functional level—the extreme picture of which may be produced by complete ablation of the gland, in other words, a state of demonstrable diminution or lack of internal secretory activity.
>
> Hyperfunction is used to indicate a condition in which all measurable abnormal function levels are of opposite sign to those pronounced by ablation.
>
> Dysfunction states are those in which evidences of hyper- and hypo-activity are simultaneously observed. Such conditions arise, for example, when endocrine organs initially hyperactive are undergoing a functional evolution to an ultimate hypo-active state. Years ago Cushing called attention to such involutions in acromegaly, and the writer and his associates have frequently observed analogous conditions in thyroid disease.

In the nomenclature of the disorders of thyroid secretion, the following terms are in general use: hyperthyroidism, synonymous with toxic goiter, exophthalmic goiter, and Graves' disease; dysthyroidism, i.e., imperfect thyroid function; and hypothyroidism, synonymous with myxedema and cretinism. The secretory disturbances of the pituitary glands, described by Cushing and others, are called hyperpituitarism, dyspituitarism, and hypopituitarism. Likewise, hyperadrenalism, dysadrenia and hypoadrenalism

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are accepted terms for describing the syndromes resulting from the excessive, irregular, or deficient secretion of adrenin (epinephrin).

The discovery of insulin by Banting,[3] and the observation that an excessive dose of insulin produces hypoglycemia with definite symptoms (Banting, Campbell and Fletcher,[4] Noble and MacLeod,[5]) made it certain that some one would recognize cases resulting from the spontaneous excessive secretion of the hormone of the pancreas, which Schaffer[6] had previously called insulin. In 1923, when nondiabetics were observed to have symptoms identical with those of an insulin reaction and found to have abnormally low blood sugars during the attacks, the question of the nomenclature of the disorders of the islands of Langerhans was considered.[7a] It was logical to regard them as analogous to the secretory disorders of other organs of internal secretion, i.e., thyroid, pituitary, and adrenals, all of which had been recognized and named, using in their terminology, the prefix *hyper* when there was excessive secretion, *hypo* when there was deficient secretion, and *dys* when the secretion was irregular; and the suffix *ism* was used to refer to the state, or action, of the organ involved. It, therefore, would seem that the disorders resulting from the excessive, uncontrolled, or deficient internal secretion of the islet cells of the pancreas should be called respectively hyperinsulinism, dysinsulinism, and hypoinsulinism, the latter to be synonymous with, but never to supplant, the long accepted term diabetes mellitus.

*Hypoinsulinism Synonymous with Diabetes Mellitus.* If diabetes mellitus, a disease due to a deficiency of insulin, had been discovered since the scientific nomenclature of disease has been adopted it would be called hypoinsulinism; but the ancient Greeks, observing polyuria, called the disease associated with it diabetes, meaning a syphon, or a fountain; and when, according to tradition, bees were seen swarming around the urine of patients from whom urine flowed like water spouting from the syphon of a fountain, the term mellitus, meaning honey, was added. Thus the term diabetes mellitus has been used since the dawn of medical history to describe the disease entity characterized by hyperglycemia, polyuria, glycosuria, and a tendency to ketosis.

Greek medical nomenclature would not be regarded as altogether scientific in the twentieth century, but the names they gave many diseases are so expressive and impressive that they have lived through the centuries; and no doubt the term diabetes mellitus will endure until the end of time. Certainly the good old name diabetes mellitus, though not as scientific as hypoinsulinism, has merit, and with sanction of long usage, it will and should be continued to be used.

Until more of practical value has been proved regarding the independent action of the pituitary, thyroid and adrenal hormones in carbohydrate metabolism, it would seem that Allen, Joslin, Banting, Opie, Cecil, Warren and others, who are regarded as authorities on diabetes, are correct in their conclusion that diabetes mellitus is essentially due to the deficient secretion

of insulin. Therefore, the term hypoinsulinism may be used correctly, except perhaps in rare cases, as being synonymous with diabetes mellitus. Granting that extra-insular influences, as the excessive secretion of the antagonistic hormones by the hypophysis, thyroid and adrenals, were primarily responsible for decreased insulin production, or availability, in diabetes the expression hypoinsulinism would be just as appropriate as if there were actual lesions of the pancreas.

*Hyperglycemia.* Hyperglycemia, regardless of its etiology, is not a disease entity and should be classified as a condition, and not a disease, of the blood. Hyperglycemia cannot be considered as being synonymous with diabetes mellitus, though it usually is a manifestation of the disease.

Hyperglycemia occurs frequently in nondiabetics. In blood sugar studies (Folin-Wu method) up to October 1, 1933, on 3076 patients, most of them routine fasting blood sugars on patients sent to us for the diagnosis and treatment of gastrointestinal and nutritional disorders, 777 were found to have hyperglycemia. Of these, according to Joslin's criteria,[9a] 535 had true diabetes mellitus leaving 242 of 2541 nondiabetics, or 9.5 per cent, who had fasting blood sugars of more than 0.120 per cent. Of these 242 hyperglycemics, in 187 the fasting blood sugars were between 0.121 and 0.140 per cent. In 36 who did not have glycosuria the blood sugars were between 0.141 and 0.160 per cent, while 19 nonglycosurics had blood sugars above 0.160 per cent. According to Priscilla White,[8] associated with Joslin, all of the 19 with postprandial blood sugar rise above 0.160 per cent should be classified as true diabetics. This would bring our series of cases of diabetes to 554 up to October 1, 1933.

There no doubt is a higher incidence of hyperglycemia in our series of cases studied than would be found in general practice, or in a general hospital, because many of the patients on whom fasting blood sugars were made were referred for suspected diabetes; but this observation shows that hyperglycemia without diabetes occurs frequently. Certainly a patient cannot be assumed to have diabetes because he has hyperglycemia of a moderate degree. There are many diseases besides diabetes in which hyperglycemia occurs.

No one would think of reporting a case of hyperglycemia, unless the term were used as a functional diagnosis, or as a qualifying term added to the name of the disease of the pancreas or other organ, which was the primary cause of the high blood sugar; yet many clinicians have reported cases of "hypoglycemia," a condition which usually results from the opposite secretory disorder of the pancreas (hyperinsulinism), and which is no more a disease entity than hyperglycemia.[7b]

*Glycosuria.* Glycosuria, like hyperglycemia, is usually a manifestation of diabetes, and is not a disease. Glycosuria, therefore, cannot be regarded as being synonymous with diabetes.

Joslin[9a] is safe and conservative in his opinion that the glycosuric pa-

tient should be considered as a real or potential diabetic until proved otherwise. He said:

> Glycosuria usually is dependent upon disease of the pancreas, particularly of the islands of Langerhans. My rule in the treatment of diabetes is to consider any patient who has sugar in the urine demonstrable by any of the common tests to have diabetes mellitus and to treat him as a diabetic until the contrary is proved. This procedure is safer for the patient, than to make use of the term glycosuria which begets indifference and may lead to disaster. It is convenient to classify patients with glycosuria, or with a history of glycosuria into four groups: true diabetics, potential diabetics, renal glycosurics, and unclassified diabetics. Under true diabetics are placed patients whose blood sugars on an unrestricted diet are 0.14 per cent or more fasting, or 0.17 per cent or more after a meal with simultaneous glycosuria which is plainly related to diet.

Joslin,[9b] however, found in a study of 6000 glycosuric patients that only 5086, 85 per cent, had true diabetes, leaving 15 per cent of nondiabetic glycosurics.

In a recent study of our records up to October 1, 1933 of routine night and morning examinations of the urine of 6641 patients, largely adults usually referred by physicians for gastrointestinal and nutritional disorders, 818 had glycosuria. Applying Joslin's criteria[9a] for establishing a diagnosis of true diabetes, i.e., the simultaneous presence of sugar in the urine, and fasting blood sugar of 0.14 per cent or more, or 0.17 per cent or more after a meal, 535 (66.6 per cent) were found to have diabetes, leaving 285 (33.4 per cent) of nondiabetics with glycosuria. Perhaps the reason why a larger percentage of glycosurics in our series were classed as nondiabetics than Joslin found in his larger series was because less than 10 per cent of our patients were diabetics, and no doubt a larger proportion of the patients referred to Joslin are sent because of actual or suspected diabetes.

Many of our nondiabetics in whom sugar was found in the routine examination of urine were studied for only one or two days, so it is probable that many of them would have been found to have true diabetes if time had been given for glucose tolerance tests. From these observations the conclusion must be drawn that glycosuria without diabetes is relatively frequent in many conditions. Glycosuria, therefore, has no place in the terminology of the disorders of insulin secretion, except as a qualifying functional diagnosis of many diseases.

Of the 181 nondiabetics in our series with moderate hyperglycemia, i.e., fasting blood sugar between 0.121 and 0.140 per cent, 29 had glycosuria. Most of this group, particularly those with both moderate hyperglycemia and glycosuria, were considered as potential diabetics. No doubt many of them would have been found to be true diabetics had the opportunity been given to make glucose tolerance tests upon them.

It is interesting to note that, up to October 1, 1933, of 218 nondiabetic patients with hypoglycemia, i.e., with fasting blood sugars below 0.080 per cent, 42 (19 per cent) had sugar in their urine. In 86 of these, in which there seems to be no doubt of the diagnosis of hyperinsulinism, 22 (26 per

cent) had glycosuria. Several of these were sent in diagnosed from the glycosuria, without blood sugar studies, as diabetes. Of 58 hypoglycemics, considered as borderline cases of hyperinsulinism, 11 (19 per cent) had glycosuria. Of 74 hypoglycemics without symptoms of hyperinsulinism, 9 (12.2 per cent) had glycosuria.

As a check, the incidence of glycosuria in conditions in which there was no evidence of disturbed insulin secretion was studied. In 576 patients diagnosed as having gastric and duodenal ulcers, in routine examination of night and morning specimens of urine, 44, a percentage of 7.8, were found with glycosuria. In 978 diagnosed as psycho-neurasthenia, usually with symptoms due to gastrointestinal neuroses, only 58, or 5.9 per cent, had sugar in their urine.

The conclusion must be drawn from these studies that glycosuria is found in many diseases besides diabetes; and that since glycosuria was found in 26 per cent of patients with hypoglycemia and symptoms of hyperinsulinism, the low renal threshold may be due to disturbed insular function.

## Hyperinsulinism

The terminology of the recently recognized disorders resulting from the assumed excessive secretion of insulin, or deficiency of anti-insulin substance, has been discussed by a number of clinicians who have reported cases of patients suffering from hypoglycemic symptoms. In the first cases reported in which nondiabetics had symptoms identical with the reaction observed in diabetics from overdoses of insulin (induced hyperinsulinism) the condition was called hyperinsulinism.[7c] A year later Cammidge [10] reported two cases of " hypoglycemia " which he assumed was due to defective glycogenesis by the liver. In November 1924 Jonas [11] cited a case of " hypoglycemia " reported by Hartman and Rieman, and reported another case, that of a diabetic who, a number of days after insulin therapy was discontinued, died in hypoglycemia (blood sugar 0.040 per cent). Jonas suggested the term " spontaneous hypoglycemia " to describe such cases. In 1925 John [12a] reported two cases of " hyperinsulinism," one of a diabetic and the other a nondiabetic, who had symptoms of hypoglycemia with low blood sugars. John concluded that " the phenomenon must be due to some irregularity, or oversensitiveness of the insulogenic regulating mechanism."

In 1927 Wilder, Allan, Power and Robertson [13] first proved pathologically the existence of hyperinsulinism. Theirs also was the first reported case of hyperinsulinism due to a neoplasm of the islands of Langerhans in which there were recurring attacks of convulsions and unconsciousness. Their classical report of the case of a physician who died in hypoglycemia from an inoperable islet cell carcinoma, which they studied at autopsy, is perhaps the most important contribution to the literature on hyperinsulinism. Finney and Finney [14] in 1928 reported the first successful resection of a large portion of the pancreas for hyperinsulinism (fasting blood sugar 0.030 per cent). The pancreas was normal in appearance and microscopic section

showed normal islet cells. The patient's blood sugar was higher after the operation, but for a time she had psychic symptoms, though she was greatly benefited by the operation. Dr. Finney states five years after the operation that she is in good health. Pribram [15] in 1928 reported three cases of "chronic hypoglycemia" and he suggested the term "glycopenia" as descriptive of such cases. Allan [16] in 1929 reported two cases of "hyperinsulinism" in which there was hypoglycemia with convulsions and unconsciousness. Resection of a portion of the pancreas by Judd [17] in one of Allan's cases resulted in improvement to the extent that the hypoglycemic symptoms were milder. Hartmann [18] in January 1929 reported a case of "idiopathic hypoglycemia" in a negro who died in a state epileptic institution. Winans [19] in 1928 reported three cases of "chronic hypoglycemia" in obese patients, which he ascribed to "overactivity of the pancreas." Waters [20] in 1929 reported three cases of "spontaneous hypoglycemia."

Carr, Parker, Grave, Fisher and Larrimore [21] in August 1931 reported a case of "hyperinsulinism" in which the hypoglycemia (blood sugar 0.042 per cent) was associated with recurring attacks of unconsciousness and convulsions. Removal of a pancreatic adenoma cured the patient. Gammon and Tenery [22] in 1931 reported a case of "hypoglycemia," "due to hyperinsulinism" and they suggested the term "dysinsulinosis" as descriptive of the condition. Marsh [23] in 1930 reported nine cases of mild "hyperinsulinism." Phillips [24] in 1931 reported a case of "hypoglycemia" in which autopsy revealed hyperplasia of the islands of Langerhans thus suggesting an organic basis for hyperinsulinism in one patient who did not have adenoma of the pancreas. A number of other cases have been reported by American clinicians, some using the term hyperinsulinism and others hypoglycemia, with various qualifying words. Derick [25] more recently reported a case of "spontaneous hyperinsulinism" due to an islet cell adenoma, in which the patient was cured by operation. Evarts Graham and Womack [26] up to December 1933 had successfully operated upon four adenomas of the pancreas, and had resected the pancreas in three additional cases of "hypoglycemia" in which adenomas were not found.

Most of the British clinicians who have reported cases, follow the lead of Cammidge, and use the term chronic hypoglycemia. Cammidge [10c] considers that chronic infections of the liver and pancreas play an important rôle in the etiology of hypoglycemia, because, as he says: "Chronic catarrh of the upper intestines is generally associated with an infection of the bile and pancreas ducts, and the consequent disturbance of the liver and pancreas may contribute to the production of a low blood sugar."

Wauchope,[27] in one of the most comprehensive reviews of the general subject of "hypoglycemia" that has been published, employs the terms "spontaneous hypoglycemia," and "functional hyperinsulinism." Wauchope's bibliography on the subject of hypoglycemia and hyperinsulinism in all its phases is one of the most extensive in the literature on this new disease entity.

Moore,[28] of Dublin, reported a case of "spontaneous hypoglycemia" which he considered as due to "insulinism." Sippe and Bostock [29] in a recent number of the *Australian Medical Journal* reported 25 cases of "hypoglycemia" and in their excellent survey they describe as "true hypoglycemia," the "fulminating types" ((a) confusional or comatose, (b) epileptiform, (c) abdominal, (d) migrainous, (e) asthmatic, (f) vertiginous, (g) cardiac) and "chronic hypoglycemia." Sippe and Bostock consider "hypoglycemia" practically as common as hyperglycemia. In a large series of cases met with in general practice (in Brisbane, Australia) the "percentage of cases of hypoglycemia was 0.47 and that of diabetes 0.51."

The first book to be written on hypoglycemia and hyperinsulinism was by a Frenchman, Jean Sigwald, entitled "L'Hypoglycémie," [30] with a foreword by Professor M. Rathery. In its 320 pages this very excellent monograph covers the literature up to 1932 on the various phases of hypoglycemia, including "spontaneous hypoglycemia," "experimental hypoglycemia," i.e., in animals by the use of insulin, and "hyperinsulinism"—"hypoglycémie par hyperpancréatie."

Most of the German medical writers who have reported cases, as Krause,[31] use the word "hyperinsulinism." One of the most comprehensive papers that has been written on the subject is by Professor Max Rosenberg [32] of Berlin on artificial and spontaneous hyperinsulinism, in which he brings out definitely that the manifestations of hyperinsulinism induced by giving excessive doses of insulin to animals and men are the same as those which occur in "spontaneous hyperinsulinism." It is interesting to note in the 141 references in Rosenberg's article how thoroughly he has covered the American literature on hyperinsulinism.

The only reference found in the Italian literature was the report of a case of "spontaneous hyperinsulinism" by Stief.[33] Three references have been found in the Scandinavian literature, one by Hagedorn [34] in which he reports two mild cases of "spontaneous hypoglycemia"; one by Ehrstrom [35] in which he reports a case of "chronic pancreatitis with hyperinsulinism"; and a third by Sjögren and Tillgren [36] who, in discussing the confusional or manic states observed in a case in which there was hypoglycemia, use the word "insulinism" to convey the idea of an excessive secretion of insulin by the pancreas.

It is evident from the various words and terms that have been used to describe the disorder due to the uninhibited, or excessive, secretion of insulin that there is need for a clarifying classification and nomenclature on this disease entity.

*Spontaneous Hypoglycemia or Hyperinsulinism?* It has been suggested that "for the present it would seem more in accordance with our actual lack of knowledge to designate all cases of hypoglycemia in which no definite proof of cause exists as spontaneous or idiopathic hypoglycemia rather than as cases of hyperinsulinism," [37] reserving the word hyperin-

sulinism for the cases of hypoglycemia in which operation, or autopsy, proves the diagnosis.

If this criterion were held necessary for diagnosis in all internal diseases, few diagnoses would be made before operation or autopsy. Apply the criterion of "proof and cause" and few cases could be diagnosed as diabetes mellitus, because, as is well known, in many cases of diabetes even the autopsy shows no demonstrable lesion of the pancreas, or other organs that may be concerned in producing hyperglycemia; yet with very few exceptions, authorities on diabetes agree that the pancreas is the essential organ involved. Except in rare cases, whenever the diagnosis of diabetes is made it is assumed that there is a deficient secretion of insulin, and no one questions the diagnosis. Why should there be a different criterion for assuming a diagnosis of hyperinsulinism in the opposite secretory disorder of the pancreas when there is hypoglycemia with symptoms that are identical with those which have been repeatedly produced by the hypodermatic administration of insulin (induced hyperinsulinism)?

It is also granted that uncontrolled release of glycogen from the liver may be a factor in hyperglycemia just as deficient glycogenesis will result in hypoglycemia; but Mann [38] has shown that it requires massive destruction of the liver to produce hypoglycemia. Mann found that permanent reduction of hepatic tissue to less than 15 per cent resulted in only slight changes in the blood sugar level. Therefore, with such enormous reserve glycogenic power it does not seem likely that in functional disorders of the liver there will be enough impairment of function to produce hypoglycemia, without other evidences of liver disorder. It, therefore, would seem that the diagnosis of hyperinsulinism is justified in those cases of spontaneous hypoglycemia in which there is no evidence of disease of the liver, pituitary, suprarenal or thyroid glands. However, the possible involvement of other endocrine organs should never be forgotten in any case in which spontaneous hypoglycemia is a manifestation, and the search for such involvement should continue as long as the patient is under observation.

Even in cases of disturbed carbohydrate metabolism due to polyglandular dysfunction the disorder should be given a name that connects it with the organ that is predominantly involved; and at this time few will question that the pancreas is the most important, if not the essential, organ in the production of the symptoms of spontaneous hypoglycemia. The term hyperinsulinism would seem to be appropriate to use in the hypoglycemia resulting from hypopituitarism, because it is a generally accepted theory that the pituitary gland controls the secretion of insulin, and when there is hypopituitarism the secretion of insulin is uninhibited and hyperinsulinism results. Cushing in a recent personal communication to the author writes: "Unquestionably all the old states that we originally described as hypophysiopriva in dogs after hypophysectomy were due to hyperinsulinism though we had no means of determining this in years gone by."

## Dysinsulinism

The name dysinsulinism was coined to characterize a condition, or disease, in which there are at times manifestations of deficient insulin secretion —diabetes mellitus (hypoinsulinism); and at other times symptoms of hyperinsulinism. In other words the term dysinsulinism is intended to describe cases in which there is unregulated, uncontrolled, or irregular, secretion of insulin, with symptoms resulting at one time from hyperglycemia and at another time from hypoglycemia.

In the nomenclature of other endocrine glands in which there is irregular or uncontrolled secretion, with both hyper and hypo phases, the prefix *dys* is commonly used, as dyspituitarism, dysthyroidism and dysadrenia. Certainly no one would dispute the correctness of the term dyspituitarism as coined by Cushing; and no one would question that there are phases of hyperpituitarism and hypopituitarism in the same patients. That the hyperpituitary syndrome frequently is followed by hypopituitary manifestations in the same patient and the latter symptoms controlled by the use of pituitary opotherapy is an accepted fact.

Rowe [2] states that he frequently has seen hypothyroidism follow hyperthyroidism, and other endocrinologists have made similar observations. The term dysthyroidism is in general use and it is found in recent editions of medical dictionaries. Dysadrenia, likewise, is an accepted word in medical dictionaries and is used by authorities on adrenal disorders. It certainly does not require much imagination to believe that there is at times irregular, or uncontrolled, secretion of the islands of Langerhans; and that in such cases there should be symptoms of diabetes and hyperinsulinism in the same patients at different times. Certainly in making glucose tolerance tests on such patients the fasting blood sugar is sometimes abnormally low, but after the ingestion of one and one half grams of dextrose per kilo of body weight there is hyperglycemia for two or three hours to be followed by hypoglycemia accompanied by typical symptoms of an insulin reaction.

The need for the term dysinsulinism was felt in January 1924 [7a] when a woman came under our observation with a history of having had diabetes for one and a half years, but showing at the time of our examination hypoglycemia with symptoms of psycho-neurasthenia. She complained particularly of "spells of quivering, with weakness and a disturbed feeling" from midnight to about 2:00 a.m. She had learned that she could get relief from the attacks by taking food; and for several months she had kept an orange on her bedside table to eat when she awakened in the night with the "spells." Her fasting blood sugar was 0.047 per cent. This patient had been on an undernutrition diet for diabetes when her nervous symptoms developed. She had reduced in weight from 210 to 160 pounds. It seems probable that the undernutrition diet this patient had been using from July 1922 to January 1924 was a precipitating factor in upsetting the insulin regulatory mechanism of the pancreas.

Joslin,[39] in 1921, called attention to the occurrence of "spontaneous hypoglycemia" in diabetics on the undernutrition diet. He reported the deaths of two diabetics that occurred while on a very low carbohydrate diet, in which the blood sugar dropped to very low levels shortly before death, i.e., 0.050 and 0.040 per cent. In commenting on these two cases he said: "The discovery of the presence of hypoglycemia during the course of treatment (of diabetes) by undernutrition is a danger signal of the first importance." It seems probable that if Joslin had seen these cases after the discovery of insulin he would have suspected that the hypoglycemia was due to the excessive secretion of insulin; and since the patients had proved diabetes, due to the deficient secretion of insulin, what term is more appropriate to describe the condition than dysinsulinism? In the last few years several similar cases have been reported and the low blood sugars have been attributed to hypersecretion of insulin (Jonas,[11] John, [12b] and Harrop [40]).

In 1930 Howland, et al.[41] reported a case of "dysinsulinism" in which there were attacks of convulsions and minor attacks resembling petit mal, and in which at times during a 24 hour study the blood sugar levels were low, 0.040, 0.041, 0.045 and 0.050 per cent. A glucose tolerance test showed a diabetic curve, i.e., 0.08, 0.25 and 0.24 per cent. They therefore pronounced it a case of dysinsulinism. Removal of a small carcinoma located at about the middle of the pancreas cured the patient clinically and the blood sugar readings had been normal for some time when the case was reported.

Nielsen and Eggleston [42] in 1930 reported three cases of "dysinsulinism," with fasting blood sugar levels of 0.050, 0.069 and 0.064 per cent. Two of these cases were completely relieved by frequent feedings and the administration of suprarenal gland orally. The third patient was improved on the same diet.

Gammon and Tenery [22] in 1931 reported the case of a women who had attacks of unconsciousness and bizarre nervous symptoms which had been called "nerves" by several physicians. Her fasting blood sugar was 0.050 per cent. A sugar tolerance test was as follows: Fasting 0.050 per cent; in 45 minutes 0.225 per cent; in two hours 0.25 per cent. There was no sugar in her urine at any time. She was relieved by diet with frequent feedings; and a year later her fasting blood sugar was still low, 0.047 per cent, but her glucose tolerance curve was nearly normal, i.e., in 45 minutes 0.125 per cent, and in two hours and 45 minutes 0.111 per cent. Gammon and Tenery suggested the term "dysinsulinosis" as descriptive of the condition of unregulated insulin secretion.

The case of "dysinsulinism" reported in 1931 by Weil [43] was most dramatic. A woman aged 29 had been overweight and developed diabetes. On a low diet the sugar disappeared from her urine but she developed attacks of convulsions and unconsciousness during her menstrual periods. She had been pronounced an epileptic. Weil found a very low fasting blood sugar

reading, 0.037 per cent. On a high carbohydrate diet with considerable quantities of sugar her blood sugar readings fell to zero, or at least so low that the colorimeter could not be read. Her diet was changed to a relatively low carbohydrate and high fat diet with frequent feedings, and her "epilepsy" has been cured. She has not had a convulsive attack in more than a year. Her recent fasting blood sugar readings were normal, i.e., 0.090, and 0.085 per cent.

More recently Love [44] reported a case in which the blood sugar readings were irregular, at times low, when the hypoglycemic manifestations were pronounced, and at other times high, when he had diabetic symptoms. An adenoma of the pancreas was suspected. Love diagnosed his case "dysinsulinism."

The above facts regarding reported cases in which patients showed evidences of uncontrolled or irregular insulin secretion, with hypoglycemia alternating with hyperglycemia, seem to justify the diagnosis of dysinsulinism as made by the authors quoted.

## Hypoglycemia

Hypoglycemia, a low concentration of sugar in the blood, is a condition —not a disease—resulting from dysfunction, or pathologic changes in the liver, or in the organs of the internal secretion concerned with carbohydrate metabolism, including the pancreas, the suprarenals, the thyroid, and the pituitary bodies. Hypoglycemia due to whatever cause, is associated with more or less characteristic symptoms depending to a great extent upon the degree of subnormal blood sugar concentration.

It is generally agreed by clinicians that the normal blood sugar concentration ranges between 80 and 120 mg. per 100 c.c. of blood. Usually no symptoms of hypoglycemia are observed until the blood sugar falls below 0.070 per cent, but below that point and to 0.060 per cent the patient complains of protean symptoms, the most characteristic of which are those described by Banting [4] and MacLeod [5] as occurring from an overdose of insulin, i.e., hunger, weakness, trembling, sweating and nervousness.

A great variety of symptoms [7c] has been described by various observers as occurring in patients with moderately low blood sugars. They include dizziness, vertigo, headaches, irritability, attacks of petit mal, lassitude, fainting attacks, tachycardia, the fatigue syndrome, the anxiety neuroses, emotional disturbances, hysterical attacks and muscular twitchings. The symptoms in different patients are at times so bizarre that they cannot be classified, the only common clinical findings being a moderately low blood sugar (from 0.060 to 0.050 per cent), and the observation that the attacks occur three or four hours after meals, particularly during the early hours before breakfast. The symptoms are relieved by taking food, and prevented by frequent feedings before the hours of expected attacks.

The symptoms of the severe degrees of hypoglycemia (blood sugar usually below 0.050 per cent) are more constant. There may be recurring

periods of mental lapses, or even psychotic symptoms, unexplained attacks of unconsciousness, muscular twitchings, and often convulsions.[7d] A number of such cases have been diagnosed, erroneously, as epilepsy, and even insanity. Recovery in such attacks may occur spontaneously, but more rapidly after the oral or parenteral administration of dextrose solutions. Coma and death may be the outcome in the most severe cases.

While hypoglycemia may be due to a functional disorder, or pathological changes in a number of endocrine glands, like its antithesis hyperglycemia, it is a clinical finding that occurs usually in the disturbed secretion of the islands of the pancreas. It should be stressed, however, that the presence of hypoglycemic symptoms in a patient with low blood sugar readings does not necessarily mean that he has hyperinsulinism; because hypoglycemia may result from deficient glycogenesis in the liver, from poisons, such as arsenicals, particularly arsphenamine, as in the case described by Cross and Blackford.[45] Other hepatotoxins as phenylhydrazine, phosphorus and the toxin of mushroom poisoning may result in such extensive damage to the liver as to disturb its glycogenic function. Likewise, acute yellow atrophy of the liver and massive tumors of the liver as in the case reported by Nadler and Wolfer[46] may cause marked hypoglycemia. Cammidge[10c] in his report of 200 cases of mild hypoglycemia considers that disturbed liver function is the important factor.

The adrenals control the mobilization of glycogen and a deficient secretion of the suprarenal glands may result in varying degrees of hypoglycemia. Anderson's[47] case in which a man had recurring attacks of hypoglycemic coma, finally dying in one, and in which the autopsy revealed a carcinoma of the cortex of the left suprarenal gland, is a striking illustration of the fact that adrenal disease can cause a severe and even fatal hypoglycemia. Rabinovitch and Barden[48] recently reported a case in which the patient died in hypoglycemic coma (blood sugar 0.025 per cent) and which at autopsy showed that the medullary portion of both adrenals was entirely replaced by lymphoid tissue. Evidently there was no secretion of adrenin. There was also a small nodule of inflammatory tissue on the tail of the pancreas, but hypoadrenalinism was considered as the important etiological factor in the hypoglycemia.

Addison's disease, of which adrenal pathology is the essential factor, is associated with hypoglycemia (Wadi,[49] and Porges[50]). Stenström[51] in 1926, reported the case of a woman who had a pronounced fatigue syndrome and unconsciousness associated with hypoglycemia. Immediate return to consciousness followed the hypodermatic administration of adrenalin. Stenström thought his case due to hyperinsulinism and hypoadrenalism. Having observed low blood pressure in some of our first cases in 1923 and 1924 we thought that while hyperinsulinism was the most important cause of the hypoglycemic symptoms, yet we considered it possible that hypoadrenalism may have been a factor in producing the abnormally low blood sugars in the cases. Ten years' experience in treating many cases of hyper-

insulinism further convinces us that hypoadrenalism not infrequently is associated with the hypoglycemia of hyperinsulinism and that it may be a factor in producing the hypoglycemia.

Thyroid deficiency (hypothyroidism) because of decreased metabolism, with insufficient utilization of glycogen, may result in hypoglycemia (Zubiram [52]). Holman [53] stressed the seriousness of the hypoglycemia, sometimes producing unconsciousness, that may appear 24 to 36 hours following operation for hyperthyroidism; and noted the immediate relief in such cases that follows the intravenous administration of glucose.

Years ago Cushing [54] called attention to hypoglycemia associated with hypophyseal tumors (hypopituitarism). More recently Joseph Wilder [55] has described what he thinks is a distinct entity, which he calls hypopituitary hypoglycemia. The gonads perhaps through their pituitary relations may be a factor in producing low sugar concentration. Weil's [43] case of the woman who had hypoglycemic convulsions only during menstruation illustrates that type.

Pluriglandular pathology, or dysfunction or hypofunction of two or more of the endocrine glands, may cause hypoglycemia, as in Patterson's [56] case of a woman who died in hypoglycemic coma. The autopsy showed a very small hypophysis and atrophy of the thyroid, adrenals and ovaries with what appeared to be a normal pancreas. Gougerot and Peyre [57] reported several cases of hypoglycemia which they thought were due to "hypoadrenalemia and dysinsulinism."

Since all types of hypoglycemic symptoms from the mildest to the most severe in which there are convulsions and coma have been produced by the injection of insulin (induced hyperinsulinism) without any other factor that could produce hypoglycemia, it surely seems that hyperinsulinism is the one most frequent cause of spontaneous hypoglycemia. Therefore, unless there are evidences of hypofunction of the other endocrine glands that play a part in carbohydrate metabolism, what has been called idiopathic, or spontaneous, hypoglycemia may safely be classified as being due to the excessive secretion of insulin by the islet cells of the pancreas (hyperinsulinism).

Even in the event that other endocrine glands are involved, certainly in all except a few cases the relatively or actually excessive secretion of insulin is the dominant factor, therefore the primary diagnosis should be hyperinsulinism; and hypoadrenalism, hypothyroidism or hypopituitarism should be added as a secondary diagnosis.

It surely seems that hypoglycemia bears the same relationship to hyperinsulinism that hyperglycemia does to diabetes mellitus (hypoinsulinism). No one would think of reporting a case of diabetes (hypoinsulinism) as hyperglycemia; neither should hypoglycemia be employed in reporting a case in which there is a low blood sugar, with the usual symptoms that may occur in hyperinsulinism.

The Quarterly Cumulative Index Medicus very properly lists hypoglycemia under the heading of blood sugar, and not as a disease entity; and it lists hyperinsulinism under diseases of the pancreas. The recently published "Standard Classified Nomenclature of Disease" [1] which is the guide for nomenclature in all teaching hospitals, does not recognize the term hypoglycemia as a diagnosis; but it accepts, and lists, hyperinsulinism as a disease under the heading of disorders of carbohydrate metabolism.

Dr. Lewellys F. Barker, Professor Emeritus of Medicine, Johns Hopkins University, noted for his accuracy in the use of words, in his new book (1934) on "Treatment of the Commoner Diseases Met with by the General Practitioner," [58] classifies "hypoinsulinism (diabetes mellitus)" and "hyperinsulinism" as endocrinopathies under the subtitle of "commoner disorders of the function of internal secretion of the pancreas." When such an ardent and discriminating philologist as Dr. Barker uses the term hypoinsulinism as synonymous with diabetes mellitus, and the word hyperinsulinism in the nomenclature of the disorders of insulin secretion, no other authority is needed for their usage by the medical profession.

Considering the data relating to the nomenclature and classification of the disorders of insulin secretion that have been presented, the use of the words hypoinsulinism (diabetes mellitus), hyperinsulinism and dysinsulinism in the terminology of the disorders of insulin secretion is logical and philologically correct.

## Conclusions

1. There is need for a clarifying classification of the secretory disorders of the islands of Langerhans of the pancreas; and the methods of nomenclature adopted in naming the disorders of other endocrine glands, i.e., the thyroid, the pituitary glands, and the suprarenal glands, should be applied in the terminology of the endocrine disturbances of the pancreas.

2. Diabetes mellitus, with few reservations, may be regarded as essentially due to an absolute, relative, or qualitative deficiency of insulin, and therefore is synonymous with, but never should be replaced by, the term hypoinsulinism.

3. Whereas it is unusual clinically to observe cases in which permanent hyperglycemia, polyuria, and glycosuria are solely or largely due to discoverable excessive secretion of the pituitary, thyroid, and adrenal glands, theoretically such cases may occur; and if recognized they should be diagnosed as pituitary diabetes, thyroid diabetes or adrenal diabetes, depending upon the dominant endocrine factor involved.

4. Hyperinsulinism best defines the disease entity characterized by hypoglycemia and resulting from an imbalance of those factors which, acting with the islands of Langerhans, ordinarily maintain the level of blood sugar within normal limits, whether the symptoms are mild, moderately severe, or severe.

5. Dysinsulinism is the term which best describes the condition in which there is irregular, unregulated or uncontrolled, insulin activity; with hyperglycemia alternating with hypoglycemia, in patients who have at times symptoms of diabetes, and at other times symptoms due to hypoglycemia not induced by exogenous insulin.

6. Hyperglycemia and hypoglycemia are not disease entities, but are temporary conditions of the blood resulting from pathological or functional changes in one or more of the organs concerned in carbohydrate metabolism. Hyperglycemia is not synonymous with diabetes and should not be used in reporting cases of illness due to deficient secretion of insulin. Neither is hypoglycemia synonymous with hyperinsulinism, and its use in reporting cases ascribed as due to the excessive secretion of insulin should be discouraged.

7. The anti-insulin action of the pituitary, thyroid and adrenal glands is an acceptable theory, but spontaneous hyperinsulinism due to conditions other than absolute or relative overactivity of the pancreas seems as difficult to prove clinically as hyperglycemia of extra-pancreatic origin. Therefore, the diagnosis of hyperinsulinism seems justifiable and advisable, in patients with hypoglycemic symptoms in whom there is no evidence of disease of the liver, thyroid, hypophysis or adrenals.

8. Even when there is multiglandular involvement in a patient with hypoglycemic symptoms, since it seems likely that in all except a few unusual cases the pancreas is the most important organ involved, the diagnosis should be hyperinsulinism, with a secondary diagnosis carrying the name of the disorder of the hypophysis, the thyroid, or the adrenals, that may also be present. In the very rare cases in which another organ is the dominant factor in producing the hypoglycemia the diagnosis of hyperinsulinism without qualification is not justifiable.

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# OBLITERATING THROMBOSIS OF THE PULMONARY ARTERIES *

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Obliterating thrombosis of the pulmonary artery or its main branches is a relatively uncommon condition if those cases which occur as a complication of surgical procedures or the puerperal state are excluded. The incidence of the condition cannot be determined from the published reports which, for the most part, appear as pathological studies on single cases. Billings [1] found 16 cases in 6200 autopsies, an incidence of 0.26 per cent, and included only those in which he felt that an embolic origin had been excluded. Six cases were found in 935 consecutive autopsies at the University Hospital, including those associated with operative procedures and septicemia. No study of a large series has been made to determine the common etiological and semeiographic features and it is for this reason that the present case is reported and the available literature reviewed. A thorough search, with the collection of all reported cases, has not been attempted. Those reports which are concerned primarily with postoperative and postpartum cases have been omitted, as have those of multiple thrombosis of the smaller branches as reported by Frothingham.[2]

## Case Report

E. F., a white male, aged 52 years, was first admitted to the University Hospital in 1929 for a hemorrhoidectomy. At that time the heart and lungs were considered to be normal and the blood pressure was 145 systolic and 95 diastolic. His second admission was in July 1932 and at this time he gave a history of having had a dry cough and a little shortness of breath on exertion for a period of about 15 years. These had not prevented him from carrying on his usual activities until May 1932 when he began to have severe paroxysms of coughing which produced extreme dyspnea. These paroxysms were brought on by talking, exertion, or respiratory irritation. Soon after this exacerbation of symptoms he began to have an afternoon fever ranging from 101° to 103° (F.). At the time of admission he had an evening temperature of 100° (rectal) which subsided after three days' rest in bed and remained normal during the remainder of his stay in the hospital. He was not cyanotic or dyspneic except with the frequent paroxysms of coughing. A few transient râles were found at the base of the right lung but aside from this the cardio-respiratory system was considered normal. The blood pressure was 140 systolic and 100 diastolic. Roentgenological examination showed some enlargement of the right hilus area and fibrosis of both lung fields. Treatment for chronic bronchitis was instituted.

He returned to the hospital in October 1932 stating that both the shortness of breath and the cough had become worse and that it was necessary for him to sit upright in order to sleep. He had had nocturnal dyspnea on several occasions and at times a feeling of substernal oppression with occasional sharp pains at the right costal margin. He had also noted palpitation and tachycardia on slight exertion but there had been no edema of the extremities. The cough had never been productive.

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The patient was extremely dyspneic and cyanotic at the time of admission to the hospital. The heart was not enlarged and, in particular, there was no increased accessibility of the right ventricle. The blood pressure was 88 systolic and 70 diastolic, whereas it had been 140 systolic and 100 diastolic 10 weeks previously. The liver dullness extended 2 cm. below the costal margin. There was no ascites or peripheral edema.

He had a constant elevation of temperature throughout the period of hospitalization, which, on one occasion, reached 104.6° (rectal). Repeated blood cultures were sterile and agglutination tests for typhoid, paratyphoid and undulant fever were negative.

Roentgenograms showed an enlargement of both hilus regions with two small areas of increased density in the right lung suggestive of infiltrative lesions. These had not been present on the previous examination and were interpreted as being embolic in origin. They gradually regressed.

The electrocardiogram was that of a right axis deviation with sharply inverted T-waves in Leads II and III and some slurring of the QRS complex. The observed vital capacity was 4500 c.c., the theoretical being 4175 c.c.

The renal concentration tests, non-protein-nitrogen of the blood and basal metabolic rate were normal. The hemoglobin dropped from 98 to 77 per cent and the erythrocytes from 5,780,000 on admission to 4,410,000. The leukocytes ranged from 14,250 to 8,000 with a normal differential count.

The dyspnea gradually improved and the patient was able to sleep with no elevation of his head. The cough became less troublesome with only occasional mild paroxysms so that he was able to talk without producing either cough or dyspnea. The cyanosis diminished but did not completely disappear. In spite of the apparent

FIG. 1. Longitudinal section through the thrombosed right pulmonary artery showing the extension of the thrombus into the branches and atelectasis of the middle lobe.

FIG. 2. Cross section through the right pulmonary artery showing complete obliteration of the lumen by the organizing thrombus.

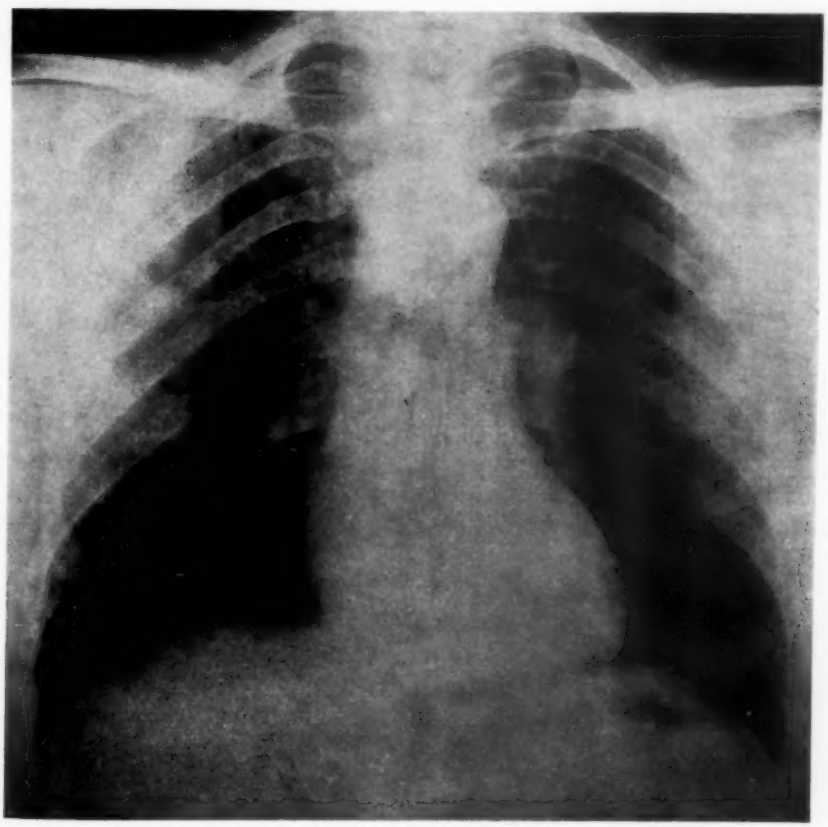

FIG. 3. Roentgenogram of chest showing dense hilus areas and a shadow in the region of the right pulmonary artery.

improvement the patient had a constant apprehensive attitude and facial expression. He was given permission to sit in a chair beside his bed but on the second occasion he suddenly became dyspneic, cyanotic and had a profuse, cold diaphoresis. He had two similar attacks within the next five hours, the third being fatal. Death occurred November 27, 1932, 46 days after admission to the hospital.

*Necropsy:* The right and left pulmonary arteries were occluded by separate thrombi which were adherent to the vessel walls. The proximal end of the thrombus in the right branch protruded into the pulmonary aorta but was not adherent in the latter region. Both thrombi extended into the branches of their respective arteries. The right pulmonary artery was completely occluded. While the thrombosis of the left pulmonary artery was not complete, the proximal end of the thrombus had apparently become loosened and folded over on itself so as to produce complete obstruction. Microscopic examination of the thrombi at various levels showed that they were firmly adherent to the vessel wall and had undergone organization. No atheromatous changes were found and the small vessels beyond the thrombi were normal. The vessel wall beneath the thrombus presented granulation and reparative fibroblastic tissue which replaced the entire thickness of the vessel wall in some sections. There were many inflammatory cells in these areas and polymorphonuclear cells were present in the more recent parts of the thrombi. The right lung weighed 800 gm., the left 620 gm. No areas of infarction were found. Both were markedly congested with only slight evidences of chronic inflammation in the large bronchi.

The heart weighed 400 gm. and the right auricle and ventricle were definitely dilated. No thrombi were found in the heart or peripheral vessels. A *Streptococcus viridans* grew in cultures taken from the thrombus. The remainder of the necropsy findings were unimportant.

## Comment

This case presents a complete occlusion of the right pulmonary artery by thrombosis and a partial thrombotic occlusion of the left. The terminal event was apparently precipitated by a detachment of the proximal end of the left thrombus which permitted it to fold on itself and completely occlude the remaining portion of the left pulmonary artery. The apparent age of the thrombi on microscopic examination was compatible with the seven months' duration of symptoms. Even though antemortem blood cultures had been sterile, a positive culture was obtained from the thrombus at necropsy. This intravascular infection was undoubtedly the etiologic agent.

Two cases of pulmonary artery thrombosis were found associated with cardiac lesions. One of these presented the usual symptoms and findings of mitral stenosis with congestive heart failure but necropsy revealed an occluded pulmonary artery in addition to the valvular defect. The symptoms of the pulmonary occlusion had been entirely masked by the cardiac lesion and its presence had not been suspected. In the second case an active endocarditis was present and necropsy revealed a large vegetation on the tricuspid valve. The thrombus in the pulmonary artery was undoubtedly of embolic origin. It had produced no recognizable symptoms in the presence of the primary cardiac disease.

Septicemia was present in three additional cases. One followed an appendectomy at which a ruptured gangrenous appendix was found. The patient died suddenly on the ninth postoperative day and a thrombosis of the

TABLE I

| Author | Sex Age | Vessel Occluded | Symptoms | Associated Pathology and Remarks |
|---|---|---|---|---|
| Rouslacroix and Perrimond [3] | M. 57 | Right main branch | Dyspnea, cyanosis, fever, cardiac decompensation | Asthma, bronchiectasis, emphysema<br>Hypertrophy of right ventricle<br>Dilatation of pulmonary aorta |
| Lutembacher [4] | | Right main branch | | Mitral stenosis |
| Barnes and Yater [5] | M. 34 | Both main trunks | Dyspnea, cough, pleural pain, cardiac decompensation | Bronchiectasis and adhesive pleuritis<br>Hypertrophy of right ventricle<br>Inverted T-wave in Leads II and III |
| Allbutt [6] | | Pulmonary aorta | Ashen pallor<br>Distressed respiration | Occurred during recovery from pneumonia |
| Dickinson [7] | M. 4½ | Main trunk and primary branches | Cyanosis<br>Respiratory embarrassment | Congenital pulmonary stenosis and patent interventricular septum |
| Eiman [8] | M. 81 | Main trunk and right branch | Chill and weakness | Thrombus in right renal artery and abdominal aorta. Dilated right heart |
| Jump and Baumann [9] | M. 48 | Main trunk and both main branches | Cyanosis, dyspnea, cough, edema. Sudden exacerbation of symptoms 3 days before death | Hypertrophy of right heart and dilated pulmonary aorta<br>Some pulmonary sclerosis<br>EKG—right ventricular preponderance |
| Means and Mallory [10] | M. 60 | Right branch | Cyanosis and dyspnea<br>Fever and leukocytosis | Hypertrophied bronchial arteries<br>Both ventricles hypertrophied |
| Ljungdahl [11] | F. 51 | Right main branch | Cough for 12 years<br>Cyanosis, dyspnea<br>Cardiac decompensation | Right heart enlarged<br>Sclerosis of larger pulmonary vessels |
| Ljungdahl [11] | F. 38 | Right main branch | Cough for 8 years. Dyspnea and cyanosis for 4 years. Severe for a few months. | Right ventricle hypertrophied<br>Thrombosis of terminal branches on left. Syphilis |

TABLE I—*Continued*

| Author | Sex Age | Vessel Occluded | Symptoms | Associated Pathology and Remarks |
|---|---|---|---|---|
| Desclin and Regnier [12] | M. 53 | Right main branch | Cough for 25 years<br>Dyspnea, cyanosis, fever, edema | Right ventricle dilated<br>Syphilitic aortitis |
| Desclin and Regnier [12] | M. 55 | Both main branches | Cyanosis, dyspnea, cough, edema. Symptoms of 4 mos. duration with sudden exacerbation 15 days before death | Thrombophlebitis of right femoral, iliac veins and vena cava |
| Stadelmann [13] | M. 27 | Both main branches | Cyanosis, fever, cardiac decompensation | Sclerosis of pulmonary artery<br>Mitral stenosis and insufficiency |
| Mönckeberg [14] | M. 56 | Main trunk and right branch. Separate thrombus in left branch | Weakness, cyanosis<br>Cardiac decompensation | Hypertrophy of right ventricle<br>Thrombus in vena cava<br>Arteriosclerosis of pulmonary vessels |
| Richter [15] | | | | Coronary artery disease |
| Neumeister [16] | | | | Chlorosis |
| Westphal [17] | | | | |
| Ittameier [18] | | Right branch | | Emphysema and pleural adhesions<br>Aortic stenosis and insufficiency |
| Tugendreich [19] | | | | Tuberculosis with caseation, and tabes dorsalis |
| Neddersen [20] | | Right and left branches | | Mitral stenosis and insufficiency |
| Brenner [21] | F. 58 | Right branch and medium sized vessels | Chronic cough<br>Cyanosis, dyspnea, and edema | Hypertrophy of right ventricle<br>Changes in vessel wall |
| Brenner [21] | F. 49 | Right and left | Chronic cough, hemoptysis<br>Cyanosis and dyspnea | Emphysema and bronchitis<br>Changes in vessel wall |

TABLE I—*Continued*

TABLE I—*Continued*

| Author | Sex Age | Vessel Occluded | Symptoms | Associated Pathology and Remarks |
|---|---|---|---|---|
| Brenner [21] | M. 58 | Many smaller branches | Sudden onset 19 months previously | Coronary artery sclerosis |
| Brenner [21] | M. 56 | Branch to right lower lobe | | Bronchitis and emphysema<br>Atheroma of pulmonary artery |
| Brenner [21] | F. 46 | Branch to right lower lobe | Dyspnea, cyanosis, edema | Mitral stenosis and atheroma of pulmonary artery |
| Brenner [21] | M. 60 | Branches to right upper and lower lobes | Dyspnea and fainting attacks | Emphysema<br>Atheroma of pulmonary artery |
| Goedel [22] | M. 59 | Main trunk and right branch | Cyanosis, dyspnea, edema<br>Cardiac failure | Right ventricle enlarged |
| Goedel [22] | M. 50 | Medium sized branches | Cyanosis, dyspnea, edema<br>Cardiac failure | |
| Hart [23] | F. | Main stem and both branches | Dyspnea, cyanosis<br>Decompensation | Hypertrophy of right and left ventricles |
| Hart [23] | M. | Main stem and right branch | | Tabes dorsalis and pyelonephritis<br>Thrombus in left crural vein |
| Boswell and Palmer [24] | M. 39 | Right and left arteries | Dyspnea, malaise, fatiguability. Sudden exacerbation of dyspnea and cyanosis | Bronchitis |
| Samek [25] | F. 63 | Right and left branches | Dyspnea, cough, cyanosis | Dilated right heart<br>Right pleural effusion<br>Thrombus of left renal and right femoral veins |
| Billings [1] | M. 50 | Both right and left branches | Weakness, pain in right chest of 10 days' duration | Bilateral hydrothorax, congestion and edema of lungs |
| Billings [1] | M. 60 | Both branches | Dyspnea and edema, cough | Chronic interstitial nephritis<br>Infarcts in both lungs, chronic pleurisy. Hypertrophy and dilatation of heart |

TABLE I—*Continued*

| Author | Sex Age | Vessel Occluded | Symptoms | Associated Pathology and Remarks |
|---|---|---|---|---|
| Billings [1] | F. | Many vessels on right Not main trunks | Dyspnea, edema and cough | 1 month postpartum at onset of symptoms. Hypertrophy of heart |
| Billings [1] | M. 50 | Thromboses of main branches on both | Dyspnea for 8 mo., worse recently. Cough. No edema | Acute pleurisy and chronic fibrous pleurisy. Hypertrophy and dilatation of heart. Thrombosed external jugular vein |
| Funke [26] | M. | Right | Marked cyanosis | Advanced pulmonary tuberculosis Tuberc. involvement of artery wall? |
| Funke [26] | M. 35 | Right | | General paresis. Gangrene of foot |
| Smith [27] | M. 50 | Right and left and extending into right ventricle | Dyspnea and edema | Pulmonary tuberculosis |
| McPhedran and MacKenzie [28] | M. 55 | Branches to right lobe | Dyspnea, cough, weakness Edema, large liver | Luetic pneumonia and arteritis |
| Russell [29] | F. 36 | Mouth of pulmonary aorta | Dyspnea and cyanosis | Pericarditis—rheumatic |
| Möller [30] | | 3 cases | | Mitral stenosis |
| Schramm [31] | F. 44 | Aorta and right branch | Dyspnea and cyanosis—5 years | Mitral stenosis |
| Pick [32] | F. 64 | Main stem and branches | | Mitral stenosis |
| Elbogen [33] | M. 44 | Main stem | | Sclerosis of pulmonary artery |
| Hoffmann [34] | M. 39 | Stem and right branch | | Sclerosis of pulmonary artery |

TABLE I—*Continued*

| Author | Sex Age | Vessel Occluded | Symptoms | Associated Pathology and Remarks |
|---|---|---|---|---|
| Förster [35] | F. 50 | Right branch | | |
| Herrmann [36] | F. 33 | Aorta and both branches | Cough, dyspnea, cyanosis, edema | Postpartum |
| Löwenstein [37] | M. 51 | Both branches | Mild cardiac symptoms for 1 year. Recent severe dyspnea and cyanosis | Patent foramen ovale, plugged by emboli<br>Proliferation of intima |
| Desclin [38] | M. 41 | Both branches | Cyanosis, palpitation and fainting for $1\frac{1}{4}$ years<br>Edema, ascites, and cyanosis | Thrombosis of right femoral vein. No sclerosis |
| Desclin [38] | F. 62 | Main stem | Cyanosis, dyspnea, and edema | Carcinoma of mediastinal lymph nodes |
| Desclin [38] | F. 45 | Main branch of right artery | Cyanosis, dyspnea, and edema | Thrombosis of right femoral vein |
| Desclin [38] | F. 49 | Main branch, right and left | Dyspnea and weakness | Thrombosis of femoral vein |
| Desclin [38] | F. 65 | Main branch of right | | Mitral stenosis<br>Thrombosis of left femoral vein |
| Desclin [38] | F. 58 | Main branch of right | | Carcinoma of esophagus |
| Desclin [38] | F. 56 | Both arteries | | Carcinoma of breast removed |
| Desclin [38] | M. 45 | Both arteries | Dyspnea and cyanosis and fainting. Bronchitis and heart trouble | Thrombosis of both femoral veins<br>Thrombophlebitis 14 years previously |
| Meldolesi and Dionisi [39] | 25 | Right | Cyanosis, dyspnea and anasarca | Mitral stenosis |
| Ferraro [40] | 23 | Right | Cyanosis and dyspnea | Mitral stenosis |
| Létulle and Jacquelin [41] | M. 58 | Right branch | Passive hyperemia | Syphilis of pulmonary artery |

left pulmonary artery was found. A *Streptococcus viridans* grew in postmortem blood cultures. The second case died 18 hours after a cystostomy, and all branches of the right pulmonary artery were found occluded by organized thrombi. A pyelonephritis and septicemia were also demonstrated. The third case was comatose on admission to the hospital and died four hours later. At necropsy pyelonephrosis and occlusion of the left pulmonary artery by an organizing thrombus were found. A *Streptococcus hemolyticus* grew on postmortem blood cultures.

## Etiology

Thrombosis of the pulmonary artery occurs most frequently as a postoperative or postpartum complication. It has also been reported [42] in association with cellulitis of the leg, severe burns, typhoid fever, malignant disease of the abdomen, and septicemia. Such cases have not been included in the table. In a study of eight postoperative cases, Glynn [43] concluded that a bacterial infection was partially responsible for the thrombus formation in all instances, but the slowing of the blood stream subsequent to their strict confinement to bed was probably a contributing factor. He did not feel that contact of the blood with an abnormal surface was of any significance in the production of the thrombus. Cohen [44] in an analysis of 35 cases also emphasized the above features but believed that previous damage to the vessel walls was important in certain instances even though infection played the leading part in the etiology. He also pointed out that pulmonary thrombosis occurs more frequently after operations below the level of the diaphragm and that it is much more frequent in adults than in children.

From an analysis of the reports covered by the above table it is seen that pulmonary artery thrombosis was associated with chronic disease of the lungs in 16 cases. These included emphysema, pleural adhesions, bronchiectasis, tuberculosis of either a caseous or fibrotic type, hydrothorax and bronchitis. This group of diseases, together with mitral stenosis, is frequently associated with pulmonary arteriosclerosis.[45] In some of these cases the arteriosclerotic process was demonstrated, in others no mention was made of the condition of the vessel wall. There were five additional instances in which only arteriosclerosis was found.

In the 62 cases covered by this table, mitral stenosis was present in 12. In this condition there is an increased pressure and a slowing of the blood stream in the pulmonary circuit with sclerotic changes in many instances. There is also the possibility of a low grade intravascular infection, or of an embolus arising from an endocardial vegetation or an auricular thrombus to account for the pulmonary thrombosis. In two cases a patent foramen ovale was found, one of which had a stenosis of the pulmonary orifice. This type of lesion produces changes in the pulmonary circuit similar to those seen in cases of mitral stenosis.

In eight cases there was thrombosis elsewhere in the venous system, in one of which the acute thrombophlebitis had occurred 14 years prior to the pulmonary thrombosis.

Syphilis was present in five cases and will be discussed in more detail later. Other less frequent conditions were cardiac failure without valvular defects (2), carcinoma of the mediastinum (2), chlorosis (1), acute endocarditis (1) and pneumonia (1). In only a few instances was the pulmonary thrombosis considered to be primary.

The immediate cause of the thrombus formation in a given case is difficult to determine and in many instances more than one possible etiological agent is present. The lodging of an embolus in a pulmonary vessel with subsequent thrombus formation is undoubtedly responsible in many instances although it is impossible to determine by microscopic examination whether or not this has been true. Möller [30] believes that an embolic origin should be assumed in all cases and this possibility should not be discarded until all possible sources of emboli have been excluded. This is the most logical explanation in those with thrombosis of a peripheral vein, mural thrombus of the right heart or endocardial vegetations.

It would seem that a blood stream infection is the most important etiological factor, particularly when the puerperal and postoperative cases are considered. In the reports analyzed it is difficult to determine the significance of infection. While many of the patients had a febrile course very few bacteriological examinations were made from either blood stream or thrombus.

Arteriosclerotic changes in the vessel walls may be important in certain instances but these changes are frequently present in the pulmonary arteries, whereas thrombus formation is relatively rare, so it is doubtful if arteriosclerosis alone is a significant etiological factor. It is possible that slowing of the blood stream in the pulmonary circulation is of greater significance. This may also be a factor in the production of pulmonary thrombosis in cardiac failure, in comatose states, as well as in postoperative cases with the patient confined strictly to bed.

The rôle of syphilis as an etiological agent is apparently a relatively minor one. Peck [46] has reviewed the literature on syphilis of the pulmonary artery and accepted only 12 cases as definitely proved. Karsner [47] reported one case with a productive-cicatricial type of lesion and discussed similar instances in the literature. In his case there was complete obliteration of the left pulmonary artery by the syphilitic lesion rather than by thrombosis. He cited the case of Létulle and Jacquelin [41] which showed a complete occlusion of the right branch by an organized thrombus. In other instances a partially occluding thrombus was present. He emphasized the fact that thrombosis is more common in the pulmonary artery than in the systemic aorta, although the syphilitic involvement of the intima is identical and explains this higher incidence in the pulmonary circuit on the basis of a slower blood flow.

A tuberculous involvement of the vessel wall by direct extension from a pulmonary focus was found in one instance. In another case an inflammatory lesion of the bronchial lymph nodes had apparently extended through the vessel wall and the acute arteritis so produced was apparently responsible for the thrombus formation. Means and Mallory [10] found a calcified mass surrounding the thrombosed pulmonary artery but there was no evidence of constriction or of underlying intimal change. They did not feel that this mass was responsible for the thrombosis.

Chlorosis is given as the etiological factor in only one instance although the possibility of this complication is mentioned in some discussions of the thrombotic tendencies of this disease. Pneumonia is mentioned by several authors as an etiological agent but only one definite example was found. Certain hypothetical agents such as circulating toxins, kinase, histamine and chemical changes in the blood have been mentioned but not demonstrated.

Karsner emphasized the association of occlusion of the pulmonary artery and tuberculosis. In five cases of syphilitic arteritis, even though the occlusion was not always complete, there was a tuberculous involvement of the lung and in one case the tuberculosis seemed to appear while the patient was under observation. He suggested that the circulatory changes contributed to the development of the tuberculous lesion.

It is interesting to note that large infarctions of the lung seldom occur following thrombus formation, which is in striking contrast to the pathologic changes frequently encountered after sudden occlusion by an embolus. This feature was specifically mentioned by many authors. In some cases small infarcted areas were found and in other instances areas of atelectasis. Passive congestion was, however, the most common pulmonary lesion. The absence of gross infarction is explained by the existence of a collateral circulation between the pulmonary and bronchial arteries. Küttner [48] has demonstrated this anastomosis and in several of the reported cases, especially that of Means and Mallory, the bronchial vessels were markedly dilated. In a few instances, as in Karsner's case of syphilitic arteritis, a collateral circulation had developed through the pleural vessels. The gradual occlusion by a thrombus permits the collateral circulation to develop, whereas this is not possible to any significant extent with a sudden occlusion.

## Symptoms

The symptomatology of pulmonary artery thrombosis is extremely variable. In certain cases it develops slowly as a terminal event in a septic patient and no symptoms referable to the thrombosis are produced. In other instances death occurs suddenly with no time for the appearance of symptoms other than the terminal cyanosis and dyspnea. When associated with cardiac failure the manifestations of the thrombosis are masked by those of the primary condition. This is particularly true in mitral stenosis in which a deep cyanosis is already present. In the majority of these cases pulmonary thrombosis is found unexpectedly at necropsy.

We are interested, primarily, in those cases in which the clinical manifestations are referable to the thrombosis alone. The early symptoms are not distinctive. They may consist of an "uneasy feeling," malaise, anorexia, palpitation and fatiguability with some shortness of breath on exertion. Many of these patients give a history of a chronic cough with a sudden intensification of symptoms a few weeks or months prior to death. This may be initiated by an acute upper respiratory tract infection or a localized infection elsewhere in the body and is generally followed by an intermittent febrile course. Cyanosis of a mild degree is common in the early stage and steadily progresses until it becomes one of the most prominent features. Shortness of breath is ordinarily present and in certain instances is the most distressing manifestation. The fact that the vital capacity of the lungs was normal in our case, in spite of the cyanosis and shortness of breath, led us to believe that there was an improper interchange of gases within the lung. Unfortunately the $CO_2$ content of the alveolar air and blood was not determined. Cough is frequently present, usually non-productive and hacking in character, and may become extremely persistent and distressing. It is to be noted that many cases in the collected reports gave a history of a chronic cough of several years' duration. In a few instances small amounts of bloody sputum have been raised, possibly as a result of small pulmonary infarctions.

Thoracic distress may occur as a dull ache which is not localized or as a sense of oppression or constriction of the chest. In others there are sharp pleural-like pains which may be associated with the slight bloody expectoration mentioned above. Allbutt called attention to the ashen pallor with the facial expression of anxiety such as is commonly seen in coronary artery occlusion.

The pulmonary findings are by no means distinctive and are most frequently those of the associated lesions. The cardiac findings are ordinarily negligible although right ventricular enlargement may ensue in long standing cases. It has been shown experimentally [49] that occlusion of the pulmonary artery produces little change in the systemic blood pressure or cardiac output until the cross sectional area of the pulmonary artery is reduced 60 per cent. Beyond this point the cardiac output is rapidly diminished and the systemic pressure drops. The fall in blood pressure in the above case is of interest in this regard.

Electrocardiograms showing right axis deviation have been reported. A sharply inverted T-wave in Leads II and III was present in our case and in that reported by Barnes and Yater.[5] These changes may suggest coronary artery disease but do not show a progressive alteration.

Roentgenological examination has revealed dense hilus areas, and in the case of Boswell and Palmer,[24] as well as our own, the shadow of the pulmonary artery was visible but not recognized as such prior to death. Although a definite diagnosis cannot be made on roentgenological examination, a prominent shadow in the region of the pulmonary artery in association

with the above clinical features should direct attention to the possibility of this condition.

Polycythemia was not a significant feature and was present in only one of the collected cases. A mild secondary anemia and a moderate leukocytosis were more common.

Right ventricular failure, as manifested by generalized edema, ascites, and enlargement of the liver, may supervene. In many instances, however, death occurs suddenly, probably because of a sudden obstruction of the remainder of the pulmonary circulation.

## Conclusions

Obliterating thrombosis of the pulmonary artery occasionally occurs as a complication of various cardiac and pulmonary conditions. In most of these cases the thrombosis has not been recognized clinically since the symptoms are masked by those of the primary disease. In a few cases the thrombosis is apparently primary and the symptoms are referable to this alone. While the manifestations are not distinctive, it is believed that in some instances the clinical diagnosis may be possible if the condition is borne in mind. Certain of these cases undoubtedly reach a quiescent stage and it is in that group that its recognition would be most beneficial.

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# PARENTERAL LIVER THERAPY IN PERNICIOUS ANEMIA: OBSERVATIONS COVERING TWO YEARS OF CONTINUED USE*

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The literature on the parenteral use of liver extract in the treatment of pernicious anemia was extensively reviewed by Conner [1] in 1932 and subsequently by others. In the main, except for the recent contributions of Murphy [2] and of Isaacs,[3] the reports which have so far appeared in the literature have to do with the parenteral use of liver extract over relatively short periods of time. In most instances the observations reported cover the effects of this form of treatment during the period of exacerbation, and therefore deal with parenteral liver therapy as an agent in the induction of remissions. It is the purpose of this paper to report the results of the continued parenteral administration of liver extract to a series of patients with pernicious anemia some of whom have been under this form of treatment for as long as two years.

## Materials and Methods

Some of the patients first came under observation while in a state of relapse sufficiently severe to necessitate hospitalization. Others had been receiving various forms of oral therapy at the return blood clinic, and were changed to parenteral treatment when this study was begun. In the main the patients included in the study were in reduced financial circumstances so that in many instances the problem of obtaining an adequate dietary was solved with great difficulty if at all.

The liver extract used was a commercial solution † of fraction G of Cohn [4] refined for parenteral administration. During the first six months of the study the extract used was of such concentration that 5 c.c. contained the material derived from 100 gm. of liver. Later the concentration of the preparation was increased so that the same amount of active material was contained in 3 c.c. of solution.[5] In all instances the injections were made intramuscularly, and in the text the term "parenterally" is used in this sense. The details of the manner of injection have previously been described.[6] Except those cases which will be specifically designated in the table, all the patients were instructed to take no liver, liver extract, kidney, or other specific anti-anemic substance during the period of study. The patients were, however, instructed to eat liberally of meat (especially red

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meat), of leafy vegetables, and of fruit. Complete obedience to dietary instructions was impossible in many instances because of poverty. During the period of treatment in the return blood clinic, at regular intervals usually not exceeding three months, an interval history was taken and a complete physical examination made. Blood counts were done frequently, the interval being determined by the status of the patient. The interval between counts rarely exceeded three months. Data were recorded on standardized forms and filed in a unit chart. The personnel of the clinic remained quite constant during the period of the study, so that in the main, observations were made by the same physicians and blood counts done by the same technical staff.

In determining the dose of extract used and the interval between treatments we were guided largely by our previous experience with this form of therapy.[6] Except in a few instances all patients were given weekly injections of the material from 100 gm. of liver for a period of at least six months. It was felt that in a large group of patients any inadequacy of this treatment would have become apparent in this time in at least some of the patients. It was realized, however, that after a state of remission has been established some patients may show no signs of relapse for a considerable period of time under inadequate therapy, or even with no treatment at all. In general the condition of a patient at the end of the six month period was regarded as satisfactory if the red cell count was about 4.5 million or above, if neurological lesions already present had shown no progression, if no new neurological signs or symptoms had become manifest, if there had been no recurrence of signs or symptoms referable to the gastrointestinal tract, and if the patient continued to enjoy a feeling of general well being.

At the end of the first six month period, the treatment of some of the patients who fulfilled the above criteria was changed so that they were given injections of the material from 100 gm. of liver every second week, instead of every week. A small group, even though their condition was regarded as satisfactory, were continued on weekly injections for a longer period as a further test of the validity of our accepted standards for adequate treatment. Subsequently the treatment of those patients whose status was satisfactory at the end of a second six month period was changed to a three, and in some instances a four week interval. At this point it must be emphasized that the plan just outlined was adopted arbitrarily merely for the purposes of this study, and is not offered of itself as a routine treatment of pernicious anemia. Since our object was to study the effects of prolonged administration of liver extract parenterally, adjuvants to the treatment were purposely omitted.

## Results and Discussion

*Red Cells.* In the table we have given the month by month red cell counts of all 38 patients included in the study. Where more than one count was done in a month, the first (not necessarily the highest) count of the

TABLE I

MONTH BY MONTH COUNTS OF ALL PATIENTS
The sex and age are given with the case number

| Date | 1 F 30 | 2 F 56 | 3 M 26 | 4 F 60 | 5 F 73 | 6 M 42 | 7 F 66 | 8 M 62 | 9 M 58 | 10 F 51 | 11 M 50 | 12 M 68 | 13 M 57 | 14 F 68 | 15 F 48 | 16 F 55 | 17 M 68 | 18 F 36 | 19 F 61 | 20 F 42 | 21 F 57 | 22 M 71 | 23 F 45 | 24 F 49 | 25 F 62 | 26 M 64 | 27 M 58 | 28 F 69 | 29 F 50 | 30 M 58 | 31 M 73 | 32 M 77 | 33 M 53 | 34 M 58 | 35 M 47 | 36 M 54 | 37 M 31 | 38 M 44 | Date |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1931 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1931 |
| July | 3.41 | 4.58 | 4.59*a* | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | July |
| Aug. | 4.18 | 4.21 | 5.28 | 3.17 | 4.25 | 2.32 | 2.44 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | Aug. |
| Sept. | 5.20 | 4.36 | 5.08 | 4.46 | 4.25 | 3.98 | 3.21 | 3.02 | 3.11 | | | | | | | | | | | | | | | | | | | | | | | | | | | | Sept. |
| Oct. | 4.82 | 4.15 | 5.33 | 4.14 | 4.16 | 4.66 | 4.01 | 4.02 | 3.67 | 4.39 | 4.91 | | | | | | | | | | | | | | | | | | | | | | | | | | Oct. |
| Nov. | 4.50 | 4.89 | 5.91 | 4.33 | 3.82 | 5.37 | 4.73 | 4.36 | 4.30 | 4.77 | 4.36 | 3.82 | 3.07 | | | | | | | | | | | | | | | | | | | | | | | | Nov. |
| Dec. | 4.56 | 5.16 | | 3.83 | 4.54 | 5.29 | 4.89 | 4.86 | 4.15 | 4.33 | 5.29 | 4.18 | 4.03 | 3.11 | 4.40 | 4.53 | | | | | | | | | | | | | | | | | | | | | Dec. |
| 1932 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1932 |
| Jan. | 4.89* | 4.85* | 5.20 | 3.79 | 5.07 | 5.41* | 4.51 | 4.43* | 4.46 | 4.40 | 4.79 | 4.53 | 5.00 | 4.70 | 4.81 | 4.41 | 4.62 | | | | | | | | | | | | | | | | | | | | Jan. |
| Feb. | 4.97 | 4.56 | | 4.22 | 4.83* | 4.86 | 4.55 | 4.99 | 4.74 | 4.91 | 5.01 | 5.25 | 5.38* | | 5.27 | 4.59 | 5.07 | 3.15 | | | | | | | | | | | | | | | | | | | Feb. |
| Mar. | 4.70 | 4.71 | 5.06 | 4.61 | 4.63 | 5.15 | 3.93 | | 4.46 | 4.95 | 4.46 | 4.91 | 5.56 | 4.90 | 5.19 | 4.87‡ | 5.42 | 4.35 | 4.34 | 4.53 | 4.42 | 4.17† | | | | | | | | | | | | | | | Mar. |
| Apr. | | | | 3.99 | | | 4.66 | 4.52 | | | | 5.81 | | | 4.36 | | 4.91 | 4.28 | 5.10 | 3.48 | 4.85 | 4.70 | 4.55‡ | 5.23 | | | | | | | | | | | | | | Apr. |
| May | 4.37 | 4.94 | | 4.22 | 4.47 | 5.10† | | | 4.31 | 5.05* | 5.17 | 5.05 | 5.32 | 4.83* | 5.35* | 5.19 | 5.02* | 4.58 | 4.89 | 4.84 | 4.86 | 4.17 | | 5.24 | 4.39 | 4.18 | 3.46 | 3.81 | | | | | | | | | May |
| June | | | | 3.81 | | | 4.82 | | 4.40 | 4.76 | | | 5.20† | 5.25 | | 4.83 | | 4.43‡ | | 5.11 | 4.56‡ | | 4.61 | 4.29 | | 4.35 | 4.89 | 3.74 | 3.84 | 4.43 | | | | | | | June |
| July | 5.04† | 4.87† | | 3.84*b* | 4.90† | | 4.82‡ | 4.84† | | | 5.04 | | | 4.42 | | | | | 4.41* | 4.68* | | | 4.78 | 5.04 | 4.73† | 4.37 | 4.74 | 4.60 | 3.83 | 4.35 | 2.76 | | | | | | | July |
| Aug. | | | | | | | | | | 4.73 | | | | | | | 5.17 | | | | 4.30 | 4.38 | | | | | | | | 3.67 | | | | | | | Aug. |
| Sept. | | | | 4.03 | | | | 4.49 | | | | | | | 4.91 | 4.36 | | 4.77 | | 4.27 | | | | | | 4.83‡ | | | 4.10 | 4.17 | | | | | | | Sept. |
| Oct. | | | | | 4.48 | 4.40 | | | | | 4.62 | | 5.48 | 4.39 | | | | | 5.08 | | | | | 5.57 | 4.15 | | 5.17† | 4.76* | | | 4.47 | 4.28 | 4.48 | 3.18 | 5.17 | 3.73 | | Oct. |
| Nov. | 4.17 | 4.76 | 4.92 | 4.22 | | | 4.44 | | | 5.04 | | | | | 4.58 | | 4.79 | | | 4.37 | 4.56 | | 4.41† | | | | | | 4.08 | 4.76* | | | | 4.23 | | 2.12 | | Nov. |
| Dec. | | | | 3.95 | 4.41 | | | | | | 4.41*d* | | | 5.90† | | 4.88 | | | | | | 5.08 | | 5.20 | 3.83 | 5.23 | | 4.01† | | | 4.09* | | 4.66 | | 4.67 | 3.65 | | Dec. |
| 1933 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1933 |
| Jan. | 5.56 | | | | | 4.90 | 4.70 | 3.06 | | 4.37 | | | 4.82 | | | | 4.97 | 4.56 | 4.98 | 4.70 | | | 5.36 | | | | 5.29 | | 4.50* | | 4.57 | | 4.49 | | | 4.41 | Jan. |
| Feb. | | 4.55 | | 3.95*c* | 4.44 | | | 3.83 | | | 4.05 | | | | 4.92 | 5.33 | | | | | | | 5.50 | 5.78 | 4.39 | | | 4.30 | | 4.60 | 4.62 | | | | 4.16 | 4.12 | | Feb. |
| Mar. | 4.25 | | | 4.65 | | | | 4.69 | | | | | 4.44 | 4.40 | | | | | | | 4.43 | | 4.50 | | 4.11 | 4.50 | 4.73 | | | 4.63 | | 4.88* | 4.35 | | | | | Mar. |
| Apr. | 4.07 | | | | | 4.67 | 4.81 | | | 4.28 | | | | | 4.82 | | 4.77 | 4.67 | | 3.93 | | 4.33 | | 4.11 | | | | | | 4.05* | | | 4.68 | 5.68 | | | 4.66 | Apr. |
| May | 4.43 | 4.34 | | 4.15 | | | | | | | 4.99 | | | | | 4.32 | | | 5.15 | | | | | 4.64 | | | | 5.37 | | 1.92 | 4.99 | | | | 4.75 | 5.35 | | May |
| June | | | 4.50 | 4.38 | | | | | | | | | | | | 4.24 | | | | | 4.45 | | 4.87 | | | | | | 4.41 | | 5.22 | 4.54 | 4.29 | | 5.36 | | | | June |
| July | | | | | 4 19 | 4 96 | 4.24 | 3.91 | | | | | 4.98 | | | | | 4.10 | | 4.67 | | 4.01 | | | | 5.00 | 4.80 | | | | | | | | | | 5.28 | July |
| Aug. | 4.46 | 4.47 | | | | | | | | 4.25 | 4.68 | | | 4.50 | | | | | | | | | | 1.87 | | | | | | | | | | 5.21 | | | Aug. |

* Two week interval begun.
† Four week interval begun.
‡ Three week interval begun.
*a* Was taking 1/4 lb. whole liver daily at time parenteral treatment was started, and continued taking whole liver.
*b* Whole liver 1/4 lb. daily added to treatment.
*c* Iron ammonium citrate 9.0 gm. daily added to treatment.
*d* Two week interval—injection of material from 200 gm. of liver (6 c.c. of extract).

month was chosen for the table. Inspection of the table at once reveals that with one exception we were not successful in maintaining a count of five million in any of the patients for even a short period of time. However, in a large majority of the patients, the counts were at or above 4.5 million most of the time. If these figures are to be compared with those recently reported by Murphy,[2] proper evaluation can be made only if the following factors are taken into account: (1) Practically one-half of our patients were in such reduced circumstances that the mere problem of existence was their major concern. (2) Except in three instances (designated in the table) no iron or whole liver was administered. (3) A sufficiently complete list of counts has been given so that all fluctuations are included. (4) Our observations cover a relatively long period of time.

*Hemoglobin.* Of the 38 patients, 21 were maintained at a hemoglobin level of 13 gm. or more per 100 c.c. of blood. In the remaining 17 the hemoglobin values ranged between 10 and 13 gm. per 100 c.c. of blood. It is possible that the exhibition of iron in large doses might have raised the hemoglobin levels in some of the patients, especially those in the lower bracket. The purpose of this study was to determine the effects of parenteral liver therapy carried over a relatively long period of time. The results of such a study might have been obfuscated had iron been employed.

*Clinical Course.* In discussing the clinical response to the treatment given, the patients may be divided into two groups: those who had been receiving other forms of therapy and were in a state of remission when parenteral treatment was started, and those who had had no previous therapy. After the red counts in the latter group had reached normal figures, their course differed in no respect from that of the former, so that no separate discussion of the latter is necessary. In no case was there any return of signs or symptoms dependent on the anemia. In no case in which neurological involvement was already present was there any progression nor did any new neurological lesions appear. If no neurological involvement was present when parenteral treatment was started, none appeared during the time the patients remained under treatment. Many patients who were bedridden at the time treatment was started regained the ability of independent locomotion, and some were able to return to useful occupations. Abnormal deep tendon reflexes did not become normal, and impaired vibratory and position sense showed no improvement in any case although in many the functional status was greatly ameliorated. Occasionally there occurred a return of acroparesthesias or glossitis, but these symptoms were always quite mild and of short duration, and bore no relationship to the condition of the blood.

*Reactions.* In our experience of close to 2000 intramuscular injections of liver extract we have encountered no severe reaction of any type, nor has a single infection resulted. In less than 0.5 per cent mild transitory reactions were noted. These usually took the form of flushing of the face, a feeling of fulness in the head and general body warmth. These symptoms

invariably passed off within a few minutes with no treatment. Pain from the injections was never a serious consideration, and no patient who was offered the alternative of returning to oral therapy (either with whole liver or liver extract) evinced any desire to change.

## Summary

1. Thirty-eight patients with pernicious anemia were treated parenterally with liver extract for periods ranging up to two years.

2. Data concerning the red cells and hemoglobin in these patients are given.

3. In a large majority of the patients the red cells remained around 4.5 million during the greater part of the period of treatment.

4. Twenty-one of the patients consistently had hemoglobin values greater than 13 gm. per 100 c.c. of blood. In the remaining 17 the hemoglobin ranged between 10 and 13 gm. per 100 c.c. of blood.

5. Clinically all of the patients remained in a satisfactory condition. A small number had mild transitory symptomatic relapses which bore no relationship to the condition of the blood.

6. No severe reaction to an injection occurred in any case.

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# MUCIN IN THE TREATMENT OF PEPTIC ULCER ASSOCIATED WITH RENAL AND HEPATIC DISEASE *

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THE usefulness of mucin in the treatment of peptic ulcer has been widely discussed for several years. The efficacy of this substance as a therapeutic agent is assumed to depend largely on its diluent and neutralizing effect on gastric acidity, and on its ability to protect gastrointestinal tissues locally against the proteolytic action of the acid gastric chyme. That it has some virtue in the treatment of peptic ulcer is strongly suggested by the brilliant results obtained by Fogelson,[1] Atkinson,[2] Brown [3] and other investigators. Our [5] experience with mucin has not been equally successful; nevertheless the striking results occasionally obtainable even in intractable [6] cases of ulcer have induced us to continue its use.

In certain types of ulcer especially beneficial results from the use of mucin are obtained. We have been of the opinion that pathologic processes which need only a favorable type of local gastroduodenal chemism to induce quiescence should the more easily and quickly heal when mucin is used in their treatment. Acute and subacute ulcers, areal inflammatory lesions, or other ulcers which may have resulted from trauma to a single tissue, together with eroding gastric chemism, should respond favorably to any treatment which renders less innocuous the aggression of such a gastric chyme. It is probable that mucin accomplishes this. In those cases, however, in which systemic, and especially neurogenic, factors contribute largely to the cause and course of the ulcer syndrome, it is doubtful whether mucin can be expected to accomplish anything more than the production of transient benefit.

When we began using mucin,[5] we noted that certain batches of this substance contained an objectionable amount of a secretogogue which when assayed showed the biologic characteristics of histamine. At present the product which has been furnished us contains much less of this secretogogue, although at times some of the samples still seem to contain an objectionable substance which accentuates gastric secretions.

One of the desirable accomplishments in the treatment of peptic ulcer, whether by surgical or medical means, seems to be reduction of gastric acidity. We have attempted to substitute mucin for alkalies in order to accomplish this, because the use of alkalies occasionally seemed to produce an increased secretory activity of the fundic glands. It is then difficult to control or materially to reduce acidity, and often the immoderate increase of

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the amount of alkalies used to accomplish neutralization will result in symptoms of toxemia.[6] Accompanying this, there will be an elevation of the concentration of urea in the blood and an increase of the carbon dioxide combining power of the blood plasma. This alkalosis is prone to complicate the treatment of peptic ulcer in the presence of associated hepatic or renal disease. It was thought that the substitution of mucin for alkalies in such cases would accomplish the desired lowering of gastric acidity without exposing the patients to the complication of alkalosis. We were, therefore, disappointed to find that frequently in precisely the type of case in which alkalosis is likely to develop, and particularly in cases in which the hepatic or renal tissues are seriously injured, the use of mucin may be productive of decidedly untoward results. The following two reports of cases are illustrative of some complicating features that may develop following the use of mucin in cases in which renal disease is associated.

### Case I

A man, aged 46 years, first came to The Mayo Clinic in 1929, because of abdominal pain which had been present for three years. A clinical and roentgenologic diagnosis of duodenal ulcer, with slight gastric retention, was made at that time. He was given medical treatment. He returned to the clinic two years later because of persistence of the duodenal ulcer and the recent development of urinary symptoms. A diagnosis of bilateral pyelonephritis with multiple cortical abscess was made. A few months later posterior gastroenterostomy was performed to relieve obstruction due to a subacute perforating duodenal ulcer. Following this, there was relief of the dyspepsia for one year, when there was a recurrence of distress occurring across the lower part of the abdomen. A diagnosis of gastrojejunal ulcer was made. The infection in the urinary tract had persisted in spite of much treatment, although the lesion did not seem to have progressed. The concentration of urea was slightly elevated, ranging from 48 to 54 mg. in each 100 c.c. of blood, which was the same as it had been a year before. An ambulatory type of ulcer diet was prescribed with 60 gm. of mucin three times a day and a small amount of alkali. One week later it was observed that the concentration of urea was 72 mg. in each 100 c.c. of blood. The use of alkali was then discontinued. Three days later the value of urea was 62 mg. and the carbon dioxide combining power of the plasma was 28 per cent by volume. It was found that discontinuance of the mucin would allow the value for blood urea to fall to its previous level, the carbon dioxide combining power to rise to normal. The administration of mucin for a few days would cause the concentration of urea to rise to 70 mg. in each 100 c.c. of blood, the carbon dioxide power to fall as low as 28 per cent by volume, and the dyspepsia to be relieved.

### Case II

A man, aged 70 years, came to the clinic because of indigestion dating back approximately three years. The indigestion had all of the characteristics of peptic ulcer. A year prior to his admission gastrointestinal hemorrhage had occurred, manifested by hematemesis, melena, syncope, and anemia. The patient also had definite evidence of coronary sclerosis, and during the course of his examination evidence of associated nephritis developed. The estimation of gastric acidity, titrated against sodium hydroxide, showed values of 98 for total and 57 for free hydrochloric acid. Fluoroscopic examination revealed a definite duodenal deformity which was assumed to be due to a peptic ulcer. The value for urea was 84 mg. in each 100 c.c. of blood;

creatinine, 2.10 mg. Examination of urine disclosed albumin, hyaline casts, and occasional erythrocytes. The carbon dioxide combining power of the plasma was within normal limits. The intake of protein was restricted to 50 gm. The patient was frequently given small amounts of milk. He responded well to a nonsurgical regimen for ulcer, which included the use of 60 grains (4 gm.) of alkali daily. The concentration of urea in the blood promptly dropped to 52 mg. After several weeks he was dismissed from observation, and advised to continue with a restricted diet, the ingestion of milk between meals, and a limited amount of alkali.

The patient continued well for four months. Then recurring gastric difficulties developed and he returned to the clinic for further examination. It was assumed that a reactivation of the duodenal ulcer had occurred. The concentration of urea was found to be 40 mg., and of creatinine 1.5 mg. in each 100 c.c. of blood. He was again hospitalized, put on a restricted protein diet with small amounts of milk at frequent intervals between meals, sedatives, and 80 gm. of mucin daily. Alkali was not used at this time. Although there was prompt improvement in the gastrointestinal symptoms, the urea in the blood soon began to increase, ranging from 46 to 72 mg. The carbon dioxide combining power of the plasma fluctuated between 64 and 48 per cent by volume. After several days slight indigestion again developed, and it was decided to supplement the mucin with 80 grains (5.2 gm.) of alkali. Within two days the concentration of urea became elevated to 82, and there was a prompt shift of the carbon dioxide combining power of the plasma to 92. It was then decided to decrease considerably the amount of the alkalies as well as of mucin, and promptly there was a drop in the carbon dioxide combining power of the plasma to 58, and within a few days the concentration of urea fell to 52.

## Comment

Similar elevation of the value for urea following the use of mucin has been noted in several other cases with associated peptic ulcer and renal disease. In such cases there is usually parallelism between the height of the value for urea and the amount of mucin used. On discontinuing administration of mucin the value for urea would promptly drop to its basic level. In several instances there was a definite drop of carbon dioxide combining power of the plasma toward the side of acidosis. There would be prompt restoration of the carbon dioxide combining power to normal when administration of mucin was stopped. One hundred grams of mucin include approximately the equivalent of 70 gm. of protein. This, when added to proteins already included in the diet of patients with nephritis, might well be the causative factor in producing elevation of the value for blood urea. Whether such elevation is due to the protein content of mucin alone is still not decided. Adding a corresponding amount of ordinary food protein to the diet of one of these patients resulted in some retention of nitrogen, but to a slightly smaller degree. It is possible, therefore, that some specific toxic derivative of protein is still contained in the mucin.

Similar untoward effects were noted in some cases of associated hepatic disease and peptic ulcer. Such patients seem to have an increased liability to the development of alkalosis when they are given enough alkali to neutralize their gastric acids. It was therefore thought that mucin might be substituted for alkalies and thus prevent the establishment of alkalosis. Definite signs of toxemia, however, resulted promptly in some of these cases

following the use of mucin. We are still uncertain regarding the exact nature of the substances contained in mucin which were responsible for these symptoms. It is, of course, possible that the protein factor alone is responsible.

## Summary

Ordinarily, if patients have uncomplicated peptic ulcer the use of 100 gm. of mucin daily does not cause changes in the value for blood urea. The use of mucin, however, if patients have ulcer and associated advanced hepatic or renal disease, should be carried on with caution, because untoward symptoms may develop during the course of the treatment. It has been our custom when such complications exist to use smaller amounts of alkalies and mucin in order to accomplish reduction of acidity. Apparently, such patients get along very well on this modified type of treatment.

The specific cause of untoward effects produced in certain cases with marked hepatic or renal disease has not been determined, although it is possible that the protein factor alone or some protein derivative is the cause of these untoward effects.

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# THE REDUNDANT DUODENUM: CLINICAL SIGNIFICANCE *

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ALTHOUGH anomalies of the duodenum are occasionally observed in the routine roentgenological examination of the gastrointestinal tract, little attention has been paid to them clinically. With the development of roentgenologic technic in gastroenterology, more of these conditions are being discovered and as a consequence their clinical significance is becoming recognized. Abnormalities of the duodenum are frequently overlooked during an ordinary barium meal study principally on account of the fact that the examiner concentrates his attention on the first part of the duodenum or cap. It is quite probable that, were the entire duodenum studied with the same meticulous care, many more instances of duodenal abnormalities would be discovered. From our study we are convinced that anomalies of the duodenum are far more common than a survey of the literature would indicate. Furthermore, we believe that with the increased attention that has recently been directed to this part of the intestine, together with the improvement in roentgen interpretation, many more cases will be discovered and their full significance understood. The roentgenological aspect of this anomaly has recently been described by one of us,[1] and in the present communication we especially direct attention to the clinical importance of this condition.

In order more fully to comprehend the significance of these malformations, it might be well to review briefly certain salient anatomical features associated with the normal duodenum. This portion of the intestine is about 10 inches in length and has a definite configuration either in the shape of an incomplete circle or in the form of a "C." Under abnormal conditions, however, it may assume bizarre forms, varying from U-shaped to V-shaped and to other obvious distortions. The first portion of the duodenum is the most mobile; the remaining portions are practically fixed and bound down by the adjacent viscera and partially by peritoneum. Although the first portion of the duodenum is the most movable it is, however, somewhat fixed by the hepato-duodenal ligament. This represents the free margin of the lesser omentum. A fold of the hepato-duodenal ligament extends down from the posterior surface of the gall-bladder to the descending portion of the duodenum. This fold is known as the hepato-colic ligament, hepato-duodeno-colic ligament, cysto-colic ligament or fold, or cysto-epiploic ligament. It is evident, therefore, that the hepato-duodenal and

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hepato-colic ligaments play an important rôle in the fixation of the superior segment of the duodenum.

In this study we desire especially to call attention to redundancy of the superior portion of the duodenum. The several ligaments originating in the fold referred to above are largely responsible for the maintenance of the looping observed in the " redundant duodenum," a term by which we have designated the condition under discussion. It is an interesting anomaly which has heretofore frequently been overlooked.

In the course of our routine roentgenological studies of the gastro-intestinal tract, we have occasionally encountered an elongation or lengthening of the superior portion of the duodenum and in all of these, a ptosis of the superior segment was noted which resulted in an anomalous loop. As a result a puddling and retardation of the contrast meal was produced and the final picture is that of a water trap in which the passage of the opaque meal appears to be delayed. Careful observation discloses definite fixation of the superior angle of the duodenum with displacement posteriorly from its normal position. In addition, the superior segment of the duodenum is likewise fixed at its anterior portion, namely at the junction of the first part or cap with the second part of the duodenum. The unusual lengthening of the superior segment results in a sagging, ptosis and looping, producing the characteristic picture of the redundant duodenum. The two fixed areas in the superior portion are well illustrated in figures 1 (B) and 2. This elongated segment of the superior duodenum varies in length from five to ten centimeters. Several types of deformities have been observed, such as the U-shaped, V-shaped, double looping and the serpentine forms. Occasionally, only a slight sagging of the elongated segment is noted. A typical illustration of a redundant duodenum is shown in figures 1 (B) and 2.

Under normal conditions the roentgen-ray examination of the duodenum presents the first portion or bulb surmounted upon the pyloric outlet, which is directed upward, slightly to the right and frequently somewhat posteriorly. This is commonly known as the superior portion and is usually not more than five centimeters in length. At the apex of the bulb or duodenal cap, the second portion is observed to form an angle with the first part and then descends downward, to the right and posteriorly. Normally, no transverse elongation of this section of the duodenum is observed. The angulation of the superior portion is easily recognized and is more or less fixed by the hepato-duodenal ligament. From this angulation the descending portion seems to take a sudden drop. However, in those instances in which the redundant duodenum is present, this picture appears quite altered. There is present a marked elongation or lengthening of the superior segment. The duodenal cap is not affected and seems to be normal in position and size. In some instances at first glance the extra loop appears as an integral part of the cap which produces the impression of an enlarged cap or diver-

ticulum. This is due to the coalescing of the extra loop with the cap shadow. However, upon manipulation no connection can be demonstrated.

The redundant duodenum with which we are here concerned usually involves the superior segment although occasionally the entire duodenum may be included. It has been variously described as a ptosis, festooning, idiopathic elongation, M-deformity or an extra looping, terms which can not be considered entirely satisfactory. It seems apparent that since the duodenum is of greater length than normal, the term redundant duodenum or dolichoduodenum should be adopted as being more accurate as well as

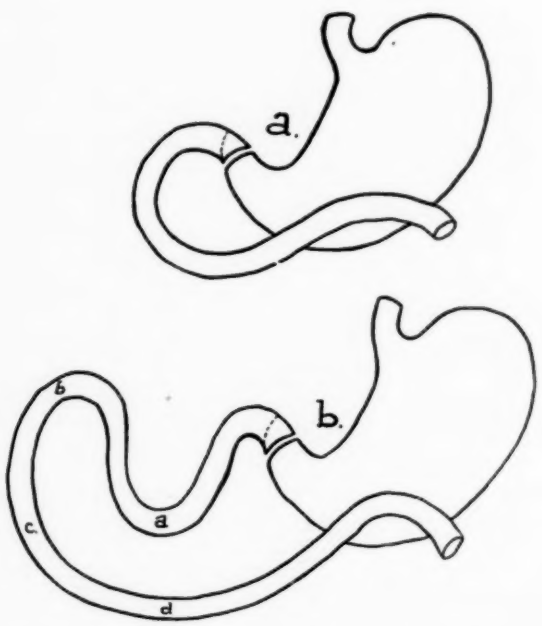


FIG. 1. *A* illustrates a tracing of the normal outline and curve of the duodenum. *B* is a tracing of a redundant duodenum, with looping at *A* shown.

descriptive. This would correspond more definitely with the nomenclature which is applied to similar conditions such as for example the redundant colon.

The literature contains but few references to this anomaly. Castronovo [2] alludes to it in describing certain malformations of the duodenum and Duval, Roux and Béclère [3] likewise refer to it. Dall 'Acqua [4] describes seven instances of mobile duodenum. He points out that in the type in which the partial mobility occurs the roentgen-ray examination revealed a double festoon or complete scroll above the fixed portion of the descending part. Kellogg,[5] Quénu and Jacquelin,[6] Brdiczka [7] and Tartagli [8] point to the occasional occurrence of this deformity. The anomaly, it can be seen,

is of considerable interest and its recognition is of some importance inasmuch as it is frequently associated with disturbances of motility of the duodenum as well as with ulceration in this area. The diminished motility with its consequent stasis, the retardation and lagging revealed in the contrast meal, all point to the important rôle which such changes may play in the production of syndromes otherwise difficult to understand. These

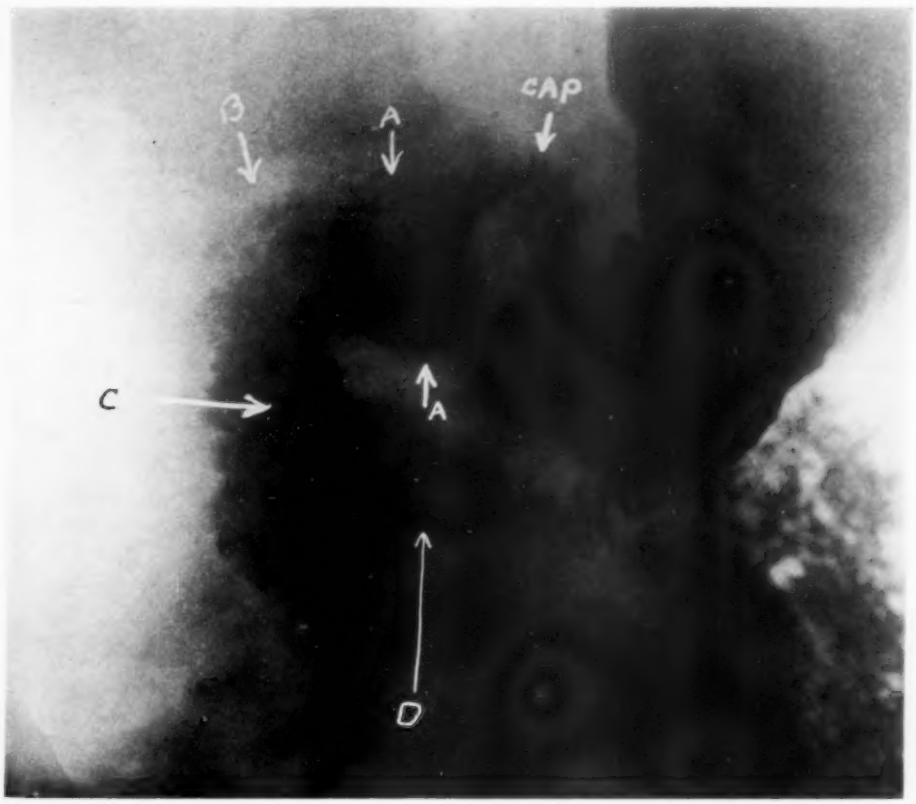


FIG. 2. Roentgenogram illustrating the lengthened superior segment of the duodenum. The duodenal cap is poorly filled on the film, but it filled well under the fluoroscope. It was markedly irritable and suggested a duodenitis. *A*—extra loop. *B*—point of fixation. *C*—descending duodenum. *D*—transverse segment of duodenum.

cases therefore merit careful study, and their early recognition is important so that effective treatment may be instituted in order to prevent the production of secondary complications.

As a result of our interest in duodenal anomalies, we have discovered 12 cases, in a series of about 500 routine gastrointestinal studies, all of which present definite elongation of the superior portion of the duodenum with sagging and looping of this segment. The ages of the patients, of which nine were male and three female, ranged between 25 and 57 years.

Important Findings in Twelve Cases of Redundant Duodenum

| Number | Name | Sex | Age | Acidity Free | Acidity Total | Loss of weight | Appetite | Pain | Nausea | Vomiting | Migraine attacks | Constipation | Complications: Ulceration Duodenal | Complications: Ulceration Gastric | Complications: Duodenal stasis | Complications: Irritable duodenum and duodenitis |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | R.I. | M | 33 | 70–90 | | + | + | 0 | + | 0 | 0 | 0 | 0 | 0 | + | + |
| 2 | B.M. | M | 53 | 55–71 | | + | + | + | + | + | + | + | + | 0 | + | + |
| 3 | C.E. | F | 31 | 24–42 | | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + |
| 4 | D.B. | F | 27 | 34–50 | | + | + | 0 | 0 | + | + | + | + | 0 | + | + |
| 5 | B.C. | M | 40 | 0–28 | | + | + | + | + | + | + | + | 0 | 0 | + | + |
| 6 | B.J. | M | 57 | 48–66 | | + | + | + | + | 0 | 0 | + | 0 | 0 | + | + |
| 7 | S.H. | M | 39 | 52–65 | | + | 0 | + | + | + | + | + | + | 0 | + | + |
| 8 | P.A. | M | 25 | 50–78 | | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + |
| 9 | G.F. | M | 46 | 54–73 | | + | + | 0 | 0 | 0 | 0 | + | 0 | + | + | + |
| 10 | W.H. | M | 26 | 27–38 | | + | 0 | 0 | 0 | + | + | + | 0 | 0 | + | + |
| 11 | R.W. | M | 35 | 68–104 | | + | + | + | + | 0 | 0 | + | 0 | 0 | + | + |
| 12 | R.E. | F | 45 | 22–54 | | + | + | 0 | 0 | 0 | 0 | + | 0 | 0 | + | + |

The symptoms are by no means characteristic. It is probable that many of these conditions exist without producing any symptoms whatever and on the other hand many symptoms no doubt arise at times as a result of an associated complication. The patient usually complains mainly of loss of appetite, nausea, discomfort in the epigastrium, vomiting, headaches and migraine attacks often of a periodic type. Abdominal pain is rarely severe and when it occurs is usually mild in character. In many instances so-called bilious attacks occur which have extended over a period of many years, often since childhood. They are frequently preceded by constipation. The constipation is replaced occasionally by intermittent diarrhea. Duodenal stasis is usually present and may account for many of the symptoms. When the attacks are frequent, loss of weight and strength supervene and in certain individuals neurasthenic symptoms become a prominent part of the symptomatology. On the other hand, remissions may occur with a disappearance of symptoms and for varying intervals the patient may enjoy comparatively good health. As a rule gastric retention does not occur in this affection and in none of our cases was gastric motility markedly disturbed. Attacks of nausea occurred in nine of our cases, vomiting in five, migraine attacks in five, constipation in nine, intermittent diarrhea in three. Pain, mild in type and not related to the intake of food, occurred in only five instances. Occasionally the liver may enlarge during an attack and tenderness may then be observed under the right costal arch. The gastric secretion is variable. In our series hyperchlorhydria occurred in seven cases, normal acidity in four and achylia in one.

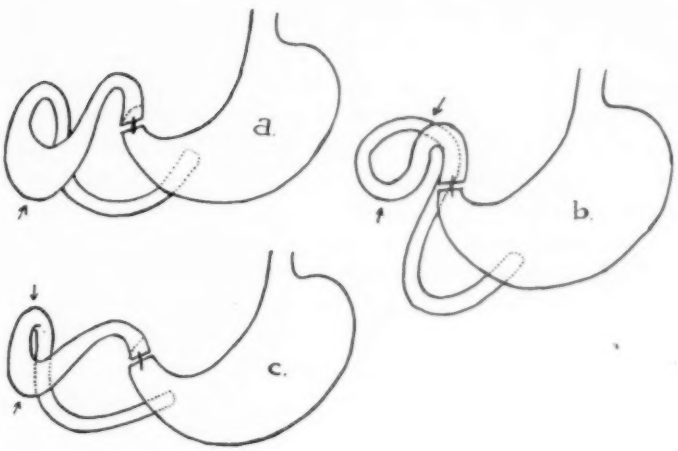


FIG. 3. Tracings of redundant duodenum *A*, *B*, *C*.

Diagrams of fluoroscopic views of the more common forms of redundancy observed in the superior portion of the duodenum. These show the posterior direction of the descending duodenum.

Duodenal dilatation and stasis is noted in the loop in *A*. *B* shows a posterior and inward displacement of the descending segment. Acute angulation with slight duodenal stasis is shown in *C*.

In order to clarify the clinical picture which may accompany redundant duodenum the following case history is presented.

### CASE HISTORY

A. P., male, aged 25 years, complained of indigestion, of 10 years' duration. The principal symptoms were nausea, regurgitation, dizziness, constipation, lack of appetite, fullness and distention after meals and discomfort in the upper right quadrant. The attacks of discomfort were at first experienced only periodically but recently they have become almost continuous. He has been living on a restricted diet and has lost 10 pounds in the past few months. On physical examination his chest was normal. The abdomen was negative with the exception of an area of distinct tenderness in the epigastrium. The test meal showed a total acidity of 78, and free HCl 50. The roentgen-ray examination was as follows: The position of the stomach is normal. There are no filling defects present. The pylorus is spastic; the duodenal cap is markedly irritable; no definite defect is observed. The superior portion of the duodenum presents a marked elongation, with a loop deformity producing a water-trap effect and resulting in a moderate degree of stasis. The colon is normal in position and incompletely filled. The diagnosis of redundant duodenum was made. The roentgenogram of this case is shown in figure 2.

From the foregoing it is evident that the redundant duodenum should be considered as a definite roentgenological entity which may be recognized by the presence of the unusual lengthening of the duodenum. Clinically, it may be significant that in our small series of cases with this anomaly peptic ulcer was frequently found and gall-bladder infections rarely so. Another interesting observation noted in this group of cases was the presence of duodenitis or marked irritation of the duodenum in those instances in which

ulceration was not present. Even when the clinical history was suggestive of ulcer, the roentgenological findings were not always corroborative. In some of these instances the picture observed was that of duodenitis or irritability of the duodenum. Duodenal retardation with stasis was observed in every instance. In our series the roentgen examination presented evidence of ulceration in five cases, duodenal in three, pyloric in one, and gastric in one. Duodenitis and irritable duodenum, which are considered by many to be precursors of actual ulcer, were found in the remaining cases. This association is not merely coincidental. It may be interpreted in the light of our present theories regarding the etiology of ulcer, as a direct effect of the redundant condition of the duodenum with its resultant stasis and consequent local injury to the mucous membrane.

In this study it seemed important to determine whether the relative positions of the stomach and colon bore any definite relationship to that of the redundant duodenum. In six instances the position of the stomach and colon was observed to be normal; in one a slight ptosis was noted; in two a moderate ptosis; in only three was a marked ptosis of the stomach and colon observed. It seems, from these findings, that the position of the stomach and colon bears no special relationship to the redundancy of the duodenum.

The diagnosis is not as a rule possible from the history and physical findings alone but must be based largely upon a roentgen-ray investigation Though the condition is best recognized under the fluoroscope, this anomaly may also be recorded on the films, when the patient is placed in the proper position. The fluoroscopic examination is usually most satisfactorily made with the patient in the upright posture, viewed antero-posteriorly, obliquely and laterally. The duodenum is best observed in the upright posture when viewed under the fluoroscopic screen. The oblique view seems to bring the entire duodenum on the screen and is the ideal position in which to visualize this condition since the duodenum in these cases is directed well posteriorly and the redundancy is often not clearly visible in the antero-posterior position. Examination should also be made routinely in the prone position. Occasionally the looping of the redundant duodenum disappears in the recumbent posture. When this occurs the serpentine appearance of the lengthened segment is observed. During the fluoroscopic examination the entire duodenum can be manipulated and the redundant segment, which may otherwise escape visualization, be brought into view. Most frequently one observes a puddling in a loop hanging from the mid-superior portion of the duodenum, between the cap and the descending sections. As has already been stated this has the appearance of a water-trap, which definitely retards the outflow of the contrast meal and which at once gives a clue as to the possibility of the presence of this abnormality. On manipulation this puddling entirely disappears, only to return with the next spurt of the opaque meal through the duodenum. In some instances

sharp angulation exists, which may cause delay in the expulsion of the contrast meal through the duodenum.

In studying this anomaly by careful roentgenological methods in the attempt to find an explanation for the double fixation of the superior duodenum the impression was gained that this may not be secondary to acquired adhesions but more probably is of congenital origin. The fixation may be due to the presence of peritoneal bands, represented by the hepatoduodenal and the hepato-colic ligaments; and the occurrence of a redundant superior duodenum is best explained upon the basis of a congenital malformation, in which the duodenum is lengthened, so that it cannot fit into the space allotted to it. The anomaly therefore seems to be dependent not only upon the abnormal fixation of the superior portion of the duodenum but also upon its unusual length.

In considering the diagnosis it should be recognized that the redundant duodenum occurs sufficiently frequently to be borne in mind in doubtful conditions involving the right upper abdomen. It is always important, however, that repeated roentgen-ray examinations be made, in order to be certain that the redundancy is permanent. These were made in the cases of our series. Since headaches associated with nausea and vomiting are often present, it is important in all obscure forms of migraine to make thorough roentgenological studies of the duodenum in order to determine any abnormality of duodenal function. In some instances, the symptoms may be attributed to gall-bladder disease, duodenal stasis, ulcer or even neurasthenia. Roentgenologically, the redundant loop may be simulated by a number of conditions such as accessory pockets of a duodenal ulcer, inverted duodenum, dilated bulb, duodenal diverticula, filled ampulla and by various other duodenal deformities resulting from adhesions in the upper right portion of the abdomen.

In the treatment of this condition conservative medical management is usually sufficient to bring about symptomatic relief, especially since in the majority of these cases periods of well being are quite characteristic. Diet plays an important rôle in the treatment. It should be of the bland type and of a high caloric content. Occasionally, it may be advisable to suggest a rest in bed of from four to six weeks, during which time general upbuilding measures, elevation of the foot of the bed, and treatment directed toward overcoming the associated conditions may be undertaken. This plan is especially indicated in those instances associated with marked enteroptosis, ulcer and the more severe grades of duodenal stasis. Transduodenal lavage with magnesium sulphate or Ringer's solution is usually very beneficial. When the symptoms are unusually severe or when adequate medical treatment no longer affords relief, surgical intervention is indicated, the most satisfactory procedure in most instances being duodeno-duodenostomy, duodeno-jejunostomy or gastro-jejunostomy. At the time of the operation a thorough exploration of the abdominal organs should be made and, depending on the patient's condition, any associated pathological lesion

that may be discovered should, if possible, be corrected. For example, if the gall-bladder is found to be diseased it should be removed, or if an ulcer is detected it should be treated according to the usual surgical procedure.

Of the 12 cases in our series, six were markedly benefited by means of the usual medical management, four were somewhat improved and in two no relief was obtained. Operation was not performed in any of our cases.

## Summary

Anomalies of the duodenum are far more common than is indicated by a survey of the literature. Of these the redundant duodenum is of considerable interest since it is frequently associated with disturbances of motility of the duodenum as well as with ulceration.

Clinically, there is no characteristic symptomatology, the picture being that of the associated lesion. Many instances undoubtedly occur without presenting any symptoms whatever.

The diagnosis is not as a rule possible from the history and physical findings alone but must be based almost entirely upon the roentgen-ray investigation.

Finally, these cases deserve careful study since their early recognition and effective treatment may prevent the occurrence of secondary complications.

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# THE HEREDITARY AND FAMILIAL FACTOR IN HYPOCHROMIC ANEMIA WITH ACHLORHYDRIA *

By William H. Barrow, M.D., F.A.C.P., *San Diego, California*

Hypochromic anemia with achlorhydria, or achlorhydric anemia, was first described by Faber [1] in 1913. During the past few years there have been much discussion and speculation in the literature in regard to this blood dyscrasia which has now been established as an easily recognizable clinical syndrome. The characteristic picture is that of an idiopathic secondary anemia occurring usually in women of middle age, the blood showing a low color index and red blood cells of small corpuscular diameters. Gastric analysis reveals an absolute achlorhydria, and there is occasionally a splenomegaly.

The familial incidence of this disease has not been discussed at length in the literature, although references are made to the occurrence of the disease in families in which pernicious anemia is also found. Witts [2] states that the occurrence of secondary anemia in female members of the family in which pernicious anemia also exists is not well known but does definitely exist, and cites cases reported in the literature. Among others he mentions a female patient, her mother and her aunt, all of whom were cases of secondary anemia. Special inquiry for evidence of familial anemia was not made in his series, but in three instances a family history of anemia was given. The mother of one patient had pernicious anemia, a sister of another had an undetermined anemia, and in another patient's family there were several cases of pernicious anemia. This last patient herself developed pernicious anemia after having had the achromic form. Witts notes that in the family histories the anemic males are apt to have a primary anemia and the females a secondary type. He suggests that the achromic anemias seem to be the equal in the female of pernicious anemia in the male. In his series there was only one male with this type of anemia.

In discussing achylia gastrica and achlorhydria Friedenwald and Morrison,[3] and Hurst,[4] mention the occurrence of this condition in several members of the same family. Hurst states that there is a familial or hereditary type of achlorhydria, which occurs, however, in not more than 2 per cent of all cases. Seventeen families are reported, with achylia present in two or more members of each family, none of whom, however, showed any evidence of anemia. He mentions other cases reported by several authors among which are instances of Addisonian anemia and simple achlorhydric anemia occurring in the same family. He believes that anemia of either form is secondary to the achylia, whether this achylia be familial or due

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to some other cause. Faber [1] advanced the theory that the achylia results in a production of bacterial toxins in the intestinal tract with a resulting hemolysis. Waugh [5] ventures the opinion that the anemia may be due to a deficiency in the gastric secretion with the absence of some substance essential to the maintenance of normal hematopoiesis.

McCann and Dye [6] suggest the possibility of a familial incidence of the disease, mentioning that one patient reported by them had a sister who presented the same symptoms of anemia, general weakness and arthritis. Heath [7] reports two cases of hypochromic anemia in women in their forties, neither one of whom gave any family history of anemia. With reference to the familial incidence of the disease he agrees that hypochromic anemia may be found in families in which other members have pernicious anemia, and he accepts the theory presented by Faber, Waugh and Witts that the anemia is gastrointestinal in origin. He advances the idea that there is possibly some substance present in normal gastric juice and absent in achlorhydria which aids in the absorption of iron.

Castle, Heath and Strauss,[8] and Morris and his co-workers,[9] have reported experimental and clinical evidence of a specific hematopoietic hormone in the normal gastric juice which is lacking in patients with primary anemia. They state, however, that the presence of this hormone is not dependent on the presence of hydrochloric acid in the juice, it being found in some cases of uncomplicated achlorhydria and in achlorhydric hypochromic anemia.

In a recent monograph on idiopathic hypochromic anemia Wintrobe and Beebe,[10] in a discussion of the familial incidence of the disease, review the cases in the literature with a familial history of anemia. They point out the not uncommon association of pernicious anemia and hypochromic anemia in the same family, and report a family history of anemia in two out of 22 of their own cases. The father of one patient had had pernicious anemia, and another patient had a cousin who had an achlorhydric form of anemia that was probably of the hypochromic achlorhydric type. Among all the cases referred to in this monograph the greatest number of cases occurring in the same generation is two, although there are two families reported which in three generations showed a larger number.

A family case history is presented herewith which is unusual because of the high incidence of hypochromic anemia in one generation.

The first member of the family to be examined was seen at the age of 42. She sought medical advice at that time because of pain and weakness of the right thumb and swelling of the right wrist. A neurological examination revealed a probable amyotrophic lateral sclerosis which accounted for these subjective symptoms, and which may or may not have been related to a long standing anemia. Neurological examination was otherwise negative except for a loss of vibratory sense over the tibiae. There was no history of menorrhagia, metrorrhagia or other blood loss. She stated that at an examination 10 years before, namely, at the age of 32, she had been found to have an anemia, and reports obtained from the physicians who had attended her at that time showed that the hemoglobin had been 58 per cent, and the red count

3.5 million. Gastric analysis had revealed an absolute achlorhydria. Otherwise except for a palpable spleen the physical and laboratory findings had been essentially negative.

At the time of my examination this patient, at the age of 42, was found to have a hemoglobin of 65 per cent, with a red count of 3.8 million. A gastric analysis, with histamine, again showed an absolute achlorhydria.

The patient was observed for a number of years and her response to iron therapy was typical of this class of case. Although rather refractory to treatment her blood count, which at one time was as low as 2.5 million with a hemoglobin of 50 per cent, was, with large doses of iron, raised to a red count of four million and a hemoglobin of 70 per cent. This improvement was preceded by an increase in the reticulocyte count from 0.1 per cent to 0.6 per cent.

The family history of this patient is of greater significance than is the report of her own case. The patient was one of six sisters, there being no brothers. The mother died at the age of 52, after several attacks of "paralysis," probably due to cerebral accidents. Although no record of any blood count is available the patient stated that her mother was always considered anemic, as were two of her mother's sisters. The father was reported as living, and as having always been in good general health.

One sister, Miss G. S., had been examined in 1919 at the age of 35 (?), because of nervousness and a somewhat persistent diarrhea. She was found at this time to have a hemoglobin of 46 per cent, with a red count of 2.7 million. A gastric analysis showed a hypochlorhydria with a hydrochloric acid of 10 degrees. There was no demonstrable etiological factor found for the anemia. The stools were negative for pathogenic parasites, and there was no history of chronic blood loss.

A second sister, Mrs. A. T., was examined in 1928, at the age of 40 (?), and was found to have a hemoglobin of 50 per cent, with a red count of 3.9 million. Gastric analysis revealed an achlorhydria. An examination a year later showed the blood to be essentially the same with the achlorhydria persisting. At the time of this second examination she complained of a menorrhagia, but this was considered to be a coincidental factor, and her condition was diagnosed as idiopathic secondary anemia.

A third sister, Mrs. A. S., was examined in 1920, at the age of 32. She complained of a menorrhagia for which she received intrauterine treatments with radium. At that time her hemoglobin was reported as 46 per cent with a red count of 3.5 million. Unfortunately I have been unable to obtain any record of a subsequent blood count. Her medical report contains no notation of any gastric analysis.

A fourth sister, Miss M. S., was examined in 1930, at the age of 24. Her chief complaints at that time were rheumatism and general debility. She was found to have a hemoglobin of 62 per cent with a red count of 4.4 million. A gastric analysis was not done.

On the fifth sister, Mrs. T. S., there were no records available of any blood counts, although she has, like her mother and aunts, always been considered anemic. There is, in her case, no report of any chronic blood loss.

A summary of these reports is given in table 1. Only one member of this family has been seen by me personally; the records of the others had to be obtained by correspondence.* The examinations in several of the cases had been made without particular study of the type of anemia encountered. There is, therefore, no conclusive evidence that all of these sisters had a hypochromic achlorhydric anemia. Nevertheless the evidence strongly suggests this possibility and in three of the cases no other diagnosis seems

* Acknowledgment is made of the help and coöperation of Dr. H. Z. Giffin of The Mayo Clinic and others in furnishing me with the clinical records of these cases.

TABLE I

Blood Counts and Gastric Analyses of a Patient with Hypochromic Anemia and of Her Five Sisters

| Name | Age | Hemoglobin (per cent) | RBC (Millions) | WBC | Differential | Gastric Analysis |
|---|---|---|---|---|---|---|
| Miss F. S. . . | 32 | 58 | 3.5 | 6,800 | Normal | Achlorhydria |
| | 42 | 70 | 3.25 | 4,000 | " | " |
| Miss G. S. . . | 35 ± | 46 | 2.7 | 6,400 | Normal | Hypochlorhydria HCl = 10° |
| Mrs. A. T. . . | 40 ± | 50 | 3.9 | 5,600 | Normal | Achlorhydria |
| | 41 ± | 45 | 4.6 | 6,500 | " | " |
| Mrs. A. S. . . | 32 | 46 | 3.5 | 7,000 | Normal | Not done |
| Mrs. M. S. . | 24 | 62 | 4.4 | 7,600 | Normal | Not done |
| Mrs. T. S. . . | No record of blood counts available but was "always considered anemic." | | | | | |

possible. In spite of the deficiencies in the completeness of the record in some of the cases anemia was present in all, and there was an achlorhydria, or marked hypochlorhydria in all cases in which a gastric analysis was performed. No other factors were constant.

One other family is reported herewith which is of interest in this discussion because any conclusions that may be drawn are at variance with those just made.

Mrs. J. VS., at the age of 28, had sought medical attention because of a three months' pregnancy. At that time she is reported to have had a hemoglobin of 32 per cent with a red count of three million. She had an achlorhydria and splenomegaly, but otherwise negative physical findings. Out of six Wassermann tests taken in the preceding five years two had been found to be positive. Three more tests were taken, however, at this time, one following a provocative salvarsan, and all were negative. She was, nevertheless, started on neosalvarsan and possibly because of this stimulus her blood count improved slightly, the red count increasing to five million and the hemoglobin to 45 per cent. She had previously failed to respond to liver therapy. When I first saw her she was complaining of general weakness and looked markedly anemic; the tongue was somewhat smooth and the mucous membranes pale. The spleen was enlarged and palpable, and the liver edge was palpable and tender. On large doses of iron her reticulocyte count increased from 2 per cent to 3.5 per cent, her hemoglobin to 89 per cent, the red count still remaining normal. There has never been any apparent cause for her secondary anemia. The clinical manifestations and the response to therapy with iron would indicate that the anemia in this case is of the achlorhydric hypochromic type.

This patient's mother, who presented no subjective symptoms, was found to have a hemoglobin of 76 per cent, a red count of 4.1 million, and a white count of 5,600. Her two children, aged less than 10, presented essentially normal blood counts.

The patient's sister, Mrs. B. W., aged 33, said that she was found to have anemia five or six years before, and that as long as she could remember she had been nervous and tired. There was no history of metrorrhagia or other chronic blood loss. She was found to have a hemoglobin of 64 per cent, a red count of 2.5 million, and a white

count of 4,600. Her liver and spleen were not palpable, and there were no neurological changes. The gastric analysis, with histamine, revealed a normal hydrochloric acid secretion.

In this family we have a case of achlorhydric hypochromic anemia with the patient's mother and sister presenting, respectively, evidence of a mild and of a moderately severe idiopathic secondary anemia of undetermined origin. A summary of these findings is given in table 2. Although a

TABLE II

Blood Counts and Gastric Analyses of a Patient with Hypochromic Anemia and of Other Members of the Family

| Name and Relationship | Age | Hemoglobin (per cent) | RBC (Millions) | WBC | Differential | Gastric Analysis |
|---|---|---|---|---|---|---|
| Mrs. J. VS. | 28 | 32 | 3 | | | Achlorhydria |
| | 28 | 42 | 5 | 4,200 | Normal | " |
| (After treatment) | 32 | 89 | 4.8 | 9,800 | " | |
| Mrs. B. W. (Sister) | 33 | 64 | 2.5 | 4,600 | Normal | Normal |
| Mrs. S. (Mother) | 55 ± | 75 | 4.1 | 5,600 | Normal | Not done |

hereditary or familial factor is suggested, there is no evidence that these three cases are related etiologically. The secondary anemias constitute a large and diversified group with overlapping morphological manifestations. Just as there was found to be not infrequently a coincidental occurrence of pernicious anemia and hypochromic anemia in the same families, so there may be a similar familial association of hypochromic anemia with other idiopathic anemias. Whether these hematopoietic disturbances could be caused by a common factor and whether this factor would be endogenous or exogenous is subject to conjecture only.

## SUMMARY

1. A review of the literature and of case histories of hypochromic anemia with achlorhydria indicates that there is a not uncommon association of this type of anemia with primary anemia in members of the same family. A family history of secondary anemia of undetermined type is occasionally found, but proved reported cases of achlorhydric anemia in more than one member of a family are rare. I have found no record of more than two cases in one generation.

2. Of possible importance from the point of view of etiology is the evidence of a familial form of achlorhydria although there is no known relationship between this and achlorhydric anemia. The specific hematopoietic hormone of normal gastric juice recently demonstrated by Castle which is absent in pernicious anemia was found to be present in some cases of achlorhydric anemia. Nevertheless, nearly all contributors to the sub-

ject, from Faber who in 1913 first described the disease, to the most recent writers, advance the theory that the anemia is secondary to a gastric secretion deficiency which results in an interference with the maintenance of normal hematopoiesis.

3. A case history of achlorhydric hypochromic anemia is presented with actual or presumptive evidence of the same type of anemia in the patient's five sisters and in her mother and mother's sisters. There is nothing in the history or physical or laboratory findings of these individuals to suggest a common factor of etiological significance. A second family is reported where there seems to be a tendency to secondary anemia, but where only one case was of the achlorhydric achromic type. If these cases are related etiologically there is again no indication as to what the etiological factor may be. One may only conclude that this type of anemia is not uncommonly found in families in which there is evidence of primary or secondary anemia in other members of the same family.

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# TUBERCULOMA OF THE BRAIN *

By Maurice Lewison, M.D., F.A.C.P., Ellis B. Freilich, M.D., and Oscar B. Ragins, M.D., *Chicago, Illinois*

In an analysis of 757 autopsies performed at the Cook County Hospital from 1917 to 1927 inclusive, on patients who had died of tuberculosis, 20 instances of the occurrence of tuberculoma of the brain were discovered. It is the purpose of this paper to present briefly certain clinical and pathologic data which have been drawn from the records of these cases. In some instances desired information has not been available. This is due in part to the fact that the condition was not usually suspected during the patients' life time, only two cases having been diagnosed ante mortem.

The literature of tuberculoma of the central nervous system is fairly extensive. Recently Anderson [1] has published an excellent review, together with a report on 27 cases, the largest single series reported.

The pathology of tuberculoma of the brain is essentially the same as that of a tuberculous lesion elsewhere. What is spoken of frequently as solitary tubercle of the brain is in reality an aggregation of many small tubercles with caseous fusion of the originally discrete lesions. Occasionally sclerosis is observed in the vicinity of tuberculoma masses. It may be constituted of proliferated glial cells or it may arise from proliferation of the adventitia of neighboring blood vessels.

From the point of view of symptomatology the cases fall into two groups. In the first the symptoms are those of a space-occupying mass in the cranial cavity or spinal canal, i.e., the symptoms of increased intracranial pressure plus those further localizing symptoms and signs which indicate the level of the lesion. In the second group of cases the outstanding clinical symptoms are those due to the coincident tuberculous meningitis; and these meningeal symptoms frequently completely mask the clinical evidences of the presence of tuberculoma.

In table 1 are given the symptoms referable to the nervous system which were present in our 20 cases on admission to the hospital. In the majority of these cases the symptoms indicated the presence of a meningitis. In seven the clinical diagnosis of tuberculous meningitis was made. In two instances tuberculoma of the brain was diagnosed. At autopsy meningitis was found in 17 cases, in one case a focal meningitis was reported, and in two cases the meninges did not show any involvement.

The sites in the brain at which the tuberculomas were found at autopsy do not indicate any special predilection of this lesion for any certain area. The incidence was somewhat higher in the left side of the brain than in the right. The number of tuberculomas found varied considerably, though over half of the cases showed a solitary lesion. There were 11 cases with

* Received for publication November 13, 1933.

TABLE I

Data of 20 Cases of Tuberculoma of Brain

| No. of Cases | Age | Sex | Color | Symptoms Referable to C.N.S. | Spinal Fluid | No. of Tuberculomas | Location of Tuberculomas | Meningitis | Clinical Diagnosis | Tuberculosis in Other Organs of the Body |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 4 | M. | C. | Neck rigidity, headache, vomiting | Increased pressure and globulin | 3 | Corpus callosum, rt. parietal lobe, left temporal lobe | Present | Miliary tuberculosis | Miliary tbc. lungs, liver, spleen, and kidneys; caseous tbc. adrenals. |
| 2 | 30 | F. | C. | Vomiting, pain in head | | 1 | Rt. parietal lobe | Absent | Tuberculous meningitis; pelvic peritonitis and salpingitis | Caseous tbc. of fallopian tubes. |
| 3 | 29 | M. | C. | | | 1 | Left temporal lobe | Present | Pulmonary tuberculosis | Bil. ulc. caseous pulmonary tbc.; nodular tbc. liver and spleen; tbc. cervical and mediastinal glands. |
| 4 | 17 | M. | C. | Headache | Increased pressure and globulin | 2 | Rt. temporal lobe, rt. middle cranial fossa | Present | Acute miliary tuberculosis; generalized skeletal tuberculosis | Tbc. pleuritis; extensive skeleton tuberculosis. |
| 5 | 34 | F. | C. | Headache | | 2 | Cerebellum, basal ganglia | Present | Pulmonary tuberculosis | Miliary tbc. lungs, spleen, liver, kidneys; caseous tbc. fallopian tubes. |
| 6 | 4 | M. | W. | Comatose condition | Increased pressure and globulin | 1 | Rt. temporal lobe | Present | None given | Miliary tbc. lungs; tbc. entero-colitis. |

TABLE I (*Continued*)

| No. of Cases | Age | Sex | Color | Symptoms Referable to C.N.S. | Spinal Fluid | No. of Tuberculomas | Location of Tuberculomas | Meningitis | Clinical Diagnosis | Tuberculosis in Other Organs of the Body |
|---|---|---|---|---|---|---|---|---|---|---|
| 7 | 16 | M. | C. | Neck rigidity | | Small multiple tuberculomas | Various parts of brain | Present | Tuberculous meningitis | Miliary tbc. lungs, pleura, pancreas, liver, spleen, ureters, bladder; tbc. abscess of small intestines. |
| 8 | 15 mo. | M. | C. | | Increased pressure and globulin | 1 | Left cerebral hemisphere | Present | Tuberculous meningitis | Miliary tbc. lungs, liver, and spleen. |
| 9 | 56 | M. | C. | Headache, neck rigidity | Increased pressure and globulin | 1 | Left cerebral hemisphere | Present | Tuberculous meningitis | Miliary tbc. lungs, liver, spleen, and kidney; tbc. ulcers of colon. |
| 10 | 5 | F. | C. | Vomiting, neck rigidity, headache pain over lt. eye | Increased pressure and globulin | 1 | Left cerebral hemisphere | Present | Tuberculoma; tuberculous meningitis | Caseous tbc. mediastinal and mesenteric lymph glands. |
| 11 | 4 | F. | Mex. | Headache | | 1 | Left cerebral hemisphere | Present | Pulmonary tuberculosis | Ulcero-caseous pulmonary tbc.; ulcers of large and small intestines. |
| 12 | 12 | F. | C. | Gradual loss of vision; headache | Increased pressure and globulin | 1 | Base of brain | Present | Tuberculoma? Tuberculous meningitis | Tbc. osteitis of sella turcica, and tracheobronchial lymph glands. |
| 13 | 45 | M. | C. | | | Multiple | Cerebellar lobes | Present | Pulmonary tuberculosis; tuberculosis of sacroiliac joint | Pul. ulcero-caseous tbc.; tbc. osteitis of sacroiliac joints; caseous tbc. adrenal and genitourinary organs. |

TABLE I (*Continued*)

| No. of Cases | Age | Sex | Color | Symptoms Referable to C.N.S. | Spinal Fluid | No. of Tuberculomas | Location of Tuberculomas | Meningitis | Clinical Diagnosis | Tuberculosis in Other Organs of the Body |
|---|---|---|---|---|---|---|---|---|---|---|
| 14 | 5 | F. | W. | Vomiting; headache | Increased pressure and globulin | 3 | Right temporal lobe, inferior occipital lobe and pons | Present | Tuberculous meningitis | Pul. ulcero-caseous tbc.; tbc. pleura, pericardium. |
| 15 | 42 | F. | ? | Vomiting; headache | Increased pressure | 1 | Right cerebellar lobe | Focal meningitis | Cerebello-pontine angle tumor | Tbc. osteitis of middle cranial fossa. |
| 16 | 28 | M. | C. | | | 1 | Pons: tuberculous abscess | Absent | Cerebro-spinal syphilis | Tbc. left apex; tbc. peritonitis. |
| 17 | 2½ | M. | C. | Rigidity of neck | | 1 | Cerebellum | Present | Encephalitis | Broncho-pneumonic pulmonary tbc.; miliary tbc. liver, spleen, and kidney. |
| 18 | 3 | F. | C. | | | Multiple | Cerebrum and cerebellum | Present | Hydrocephalus | Tbc. ulcers of rectum; caseous tbc. uterus and fallopian tubes. |
| 19 | 45 | F. | C. | Nausea; headaches | Increased pressure; Wassermann ++ | 2 | Not stated | Present | Cerebro-spinal syphilis | Bilateral ulcero-caseous tbc.; caseous tbc. mediastinal and abdominal lymph glands; miliary tbc. liver, spleen, and parametrium. |
| 20 | 24 | M. | Mex. | | | 2 | Rt. parietal lobe, and cerebellum | Present | Epidemic meningitis | Miliary tbc. lungs, liver, spleen; caseous tbc. tracheo-bronchial lymph glands. |

one tuberculoma, four cases with two, two cases with three, and three cases with multiple tuberculomas.

In all of these 20 cases tuberculous lesions were found in other organs of the body in addition to the lesions of the brain. The occurrence of brain tuberculoma in the various clinical types of tuberculosis in our series is shown in table 2.

TABLE II

| Clinical Type of Tuberculosis | No. of Cases | Incidence of Tuberculoma |
|---|---|---|
| Pulmonary tuberculosis | 482 | 4 |
| Miliary tuberculosis | 96 | 1 |
| Tuberculous meningitis | 146 | 12 |
| Tuberculous peritonitis | 32 | 2 |
| Addison's disease | 1 | 1 |

The youngest case in our series was 15 months and the oldest 56 years. The average age was 22.7 years. It was predominantly an adult group. This age incidence in our series is of interest since it is often stated that brain tuberculoma occurs with greatest frequency in childhood. There was an equal number of males and females in the group. There were 16 cases in colored patients, two in white and two in Mexicans. The high proportion of colored patients is perhaps significant.

## CONCLUSIONS

1. Twenty instances of tuberculoma of the brain were discovered in 757 autopsies of tuberculous patients.
2. The clinical signs and symptoms of meningitis frequently masked the tumor syndrome which may be presented by these cases.
3. The average age in these 20 cases was 22.7 years: it was a predominantly adult group.
4. Nearly one-half (45 per cent) of these cases showed the presence of more than one tuberculoma.
5. All parts of the brain seem equally subject to the development of tuberculoma.
6. Tuberculous foci in other portions of the body were uniformly present.

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# EDITORIALS

WHAT constitutes leadership in medicine? Leadership is the ability to inspire a desire for improvement and the willingness to work to that end. A leader in medicine not only gives instruction but makes of that instruction an inspirational force that leads the listener to study for himself and to remain ever unsatisfied with his own knowledge. Inspirational leadership in medicine comes largely from a personal magnetism in one with a broad knowledge of the science and art of medicine. To get it one must see and hear the leader. Reading what he writes falls short of inspiration. This is why we go to medical meetings. How much easier to stay at home and read the published paper, but how much less vivid, less stimulating, less worth while is it to read rather than to hear and see the leader in his presentation of a medical topic.

HENRY A. CHRISTIAN, M.D., F.A.C.P.

## *PSYCHOANALYSIS*

OF WHAT use, in the treatment of the patient, is psychoanalysis? This is a question which must have occurred to many a physician. Nor can he readily find a dependable answer. It is by results, especially end-results, that we should judge the merit of any form of therapy. Because of scarcity of such information in the case of therapeutic psychoanalysis, physicians have assumed an attitude toward that procedure all the way from open hostility to wild enthusiasm, with hostility or indifference predominating.

That many physicians should look askance at psychoanalysis is due in part to the seeming bizarreness of some of the tenets of the cult, and in part to doubt as to the good sense and judgment of the analysts. Certain affectations on their part shake confidence. When, as a group, they attain to greater maturity, they will inspire more faith. The young analyst is often a zealot. Like a convert to a new religion, he becomes narrowly sectarian. The strict Freudian sees no good in heterodox activities. This is all rather a pity because unquestionably psychoanalysis has much that should be of vital interest to the physician.

There are at least three purposes to which psychoanalysis can be put. These are psychological research, education and therapeutics. Of its value in the first of these, there can be no doubt. In the exploration of the human mind the psychoanalytical technic has penetrated new depths. It has revolutionized our notions of mental anatomy. Also, in education, it has proved its worth. For those who seek to solve problems of personality, a true knowledge of self is indispensable. It is well for any type of psychodiagnostician or therapeutist to know his own blind spots, conflicts and prejudices. It may be accepted that these can be discovered more completely by psychoanalysis than in any other way.

There still remains, however, for the practicing physician the question: has psychoanalysis any place in the actual care of the sick? Only data upon the outcome in clinical cases can truthfully answer this question. The recent paper of Kessel and Hyman * is very important because it contains such information. These physicians referred certain patients to psychoanalysts and observed whether the analysis accomplished the purpose for which it was undertaken. In slightly over 50 per cent of their cases, patients were helped; in 15 per cent they obtained cures which they regarded as specific, that is to say obtainable in no other way. It is upon the basis of data of this kind that physicians will ultimately achieve a sound evaluation of the method. It is to be hoped that much more will presently be published, and that, too, in the journals commonly read by clinicians.

That 15 per cent of "specific" cures were obtained by Kessel and Hyman is ground for looking upon the treatment as important. That not a greater percentage of the cases treated gave good results indicates either that the treatment was poorly given or that the patients were badly selected. Improvement in technic is a problem for the analyst. Improvement in the selection of cases is a problem for the physician.

At the present time we have but few guides to selection. Patients will fall, of course, for the most part in the general group of so-called neurotics or poorly adjusted persons. Also, it seems clear that a high degree of intelligence is a requisite, and that the patient be not too old; also that he have an understanding of the nature of the technic and a willingness to be analyzed. But we need far more explicit guides than these in selecting cases.

The availability of the treatment is a very large factor. The orthodox analysis is very time-consuming and expensive, and on that ground alone impossible for many persons who seemingly may need it. In a general hospital or dispensary, because of its very cumbersomeness, it is useless as a form of routine treatment for patients of a certain type.

In hospitals, however, where clinical research is done, psychoanalysis will find its place. It will be used not for the immediate purpose of curing patients, though it may do that, but to widen our knowledge of disease. It may be expected, through the increased understanding it gives us of the nature of disease, to permit improvements in many forms of therapy. We shall understand the patient and his reactions to his disease better in the light of knowledge gained through psychoanalytical research, and so be able to treat him better, even though formal therapeutic analysis is used but seldom or not at all. It is likely that new forms of treatment will emerge, the sort that Stekel † calls active analysis, in contrast to the passive type of the orthodox school, which while preserving the essence of the analytic theory will be so simple and direct as to be available to the host of patients

* KESSEL, L., and HYMAN, H. T.: The value of psychoanalysis as a therapeutic procedure, Jr. Am. Med. Assoc., 1933, ci, 1612.

† STEKEL, W.: The future of psychoanalysis (translation by L. S. LONDON), Psychoanalytic Rev., 1933, xx, 327.

needing such treatment, but to whom formal analysis is barred. Also, as Stekel brings out, the psychoanalytic type of understanding may come to permeate all medical practice. It will become the possession of all physicians, not merely of a small group of specialists. Because of all this, it is greatly to be desired that physicians substitute, for an attitude of hostility or indifference, one of active interest, careful checking of results, and finally constructive criticism.

JAMES H. MEANS

# REVIEWS

*Metabolic Diseases and Their Treatment.* By ERICH GRAFE; translated by MARGARET GALT BOISE, under the supervision of EUGENE F. DUBOIS, M.D., and HENRY B. RICHARDSON, M.D. xii + 551 pages; 16 x 24 cm. Lea and Febiger, Philadelphia. 1933. Price, $6.50.

It is a genuine pleasure to welcome the appearance of an English translation of this well-known German work on the diseases of metabolism. The material has been carefully selected and attractively presented. The references are abundant, judiciously chosen, and generally accurate. The German literature is naturally widely covered, but the important American and French work is also well represented and properly appraised and credited. Throughout the book the author displays exceptional powers of lucid yet pithy exposition. The sections of the book on obesity and on diabetes are of particular interest. There are fundamental differences from the orthodox American conceptions, particularly as regards therapy, and many of these are stimulating and refreshing. That many will be inclined to differ sharply from the author in matters of detail is quite evident, but this in no way detracts from the educational value of this book. Dr. DuBois and Dr. Richardson have done a valuable service by their careful supervision of this excellent translation. It seems to the reviewer that it is one of the best textbooks on disorders of metabolism which has appeared in recent years. He will have no hesitation in recommending the book to students as probably the best short treatise available at the present time in the field of metabolic diseases.

G. A. H.

*Behind the Doctor.* By LOGAN CLENDENING. xxviii + 458 pages; 16.5 x 24 cm. Alfred A. Knopf, New York. 1933. Price, $3.75.

*The Great Doctors.* By HENRY E. SIGERIST; translated from the German by EDEN and CEDAR PAUL. 436 pages; 15 x 22 cm. W. W. Norton, New York. 1933. Price, $4.00.

It seems that every one who touches medical history, whether he be a mere dabbler or a university professor of the subject, is immediately seized with a desire to write a popular book on the subject. There have been many of such books of late years, some good, some bad and some indifferent. It is no mean task to try to compress the whole of medical history in a few pages and to make it understandable and interesting to a layman, and it requires peculiar talents which the authors of both the above books are fortunate enough to possess.

The first is written by a master of journalese, who has gleaned many an interesting tale from the past and made a book which will delight not only the doctor familiar with medical history, but also the one who knows nothing about it and the layman who wishes to know something of what lies behind the doctor. To the last it will come as a revelation and it reads like a thrilling, best selling novel. The subject of the healing art from the medicine of primitive man to the modern doctor with his vitamins and roentgen-rays and his new chemicals is satisfactorily covered, especially from a layman's standpoint. The tale is told with great gusto and imaginary conversations enliven what otherwise might be a mere recital of facts. The paragraphs are short and the tempo of the book *allegro con moto* and at times *prestissimo*. The book is profusely illustrated with, for the most part, well chosen pictures, portraits, and drawings. Many of them unfortunately are poorly reproduced.

The second book is a biographical history of medicine and the story is told around the lives of 48 men whom Sigerist evidently thinks either the most interesting or the

most important. It was originally written in German but the translators, old hands at the game, have done a good job.

In his preface, the author forestalls any criticism of his choice of the men he has portrayed and that certainly is his affair, but many estimates seem strange. Soranus comes in for his share of the book, but no mention is made of his pediatric text which is perhaps the best of the ancient ones and two-thirds correct, judged by present-day standards. Roentgen, who changed modern diagnosis, gets but a short paragraph. In the German edition no Americans are given any more than a passing notice and in the second only Osler is added as a sort of sop to American readers. Morton and anesthesia; Walter Reed and his co-workers and Gorgas making the tropics safe for white men; Beaumont and his contribution to physiology; Halsted and his work especially local anesthesia, Marion Sims, O'Dwyer and many others would seem worthy enough to be the center of a chapter. The book is interesting, chiefly as an exposition of the views of one of the most eminent living medical historians, and his estimates and how he adjudges the great men of the past are not to be taken lightly. The illustrations are excellent and well produced. Both books contain extensive bibliographies and it is striking how both, using different sources, have given essentially the same picture of Vesalius and his achievements, good evidence of the crystalization of our knowledge of the man and his work. Both books may be recommended.

J. R.

*Die Venarum Ostiolis, 1603, of Hieronymus Fabricius of Aquapendente (1533?-1619).* Translated by E. J. FRANKLIN, D.M. 98 pages; 16.5 x 25 cm. Charles C. Thomas, Springfield. 1933. Price, $3.00.

Here is a book to delight the heart of the bibliophile, a facsimile edition of this comparatively little known work with an introduction, translation and notes by one who knew what he was about. The valves in the veins had been noted before but no one had paid much attention so that Fabricius deserves the credit of putting them before the profession. Among his many students in anatomy was William Harvey; the valves in the veins set him thinking and the result was his discovery of the circulation of the blood. It is a well planned book containing a biography, a history of the early work on the venous valves, an account of the theatre of the school of anatomy at Padua and some extremely useful bibliographical notes. The original plates have been reproduced. Every library should have this book and also every one interested in the history of medicine. It is beautifully printed on good paper and is a credit both to Dr. Franklin and to the publisher.

J. R.

*Mental Hygiene in the Community.* By CLARA BASSETT. The Macmillan Company, New York. 1934. Price, $3.50.

*Mental Hygiene in the Community,* published in January 1934, is written by one trained and experienced in psychiatric social work. It is a panoramic exposition of available data aiming to present in brief and correlated form the various ways in which mental hygiene may be of importance and value, and where it may profitably function in the present organization of community life. The book should stimulate interest and encourage experimentation for meeting local mental health needs and situations. Each chapter contains pertinent suggestions for preliminary study and investigation of specific phases of the problem and illustrations of methods that are applicable for experimentation.

The author views the present status of mental hygiene as being unable to offer definite and concrete solutions for the many problems involving the amelioration, treatment, or cure of the multiple adverse mental and personality situations or their prevention; or the promotion of positive mental health, the latter depending on forces

lying partly outside the question of illness and its avoidance. The contributions that law, psychology, sociology, education in its broadest sense, or public policies must make in the latter field cannot avoid the fundamental place which modern medicine occupies or may be expected to occupy in the future, for the promotion of good mental health implies a knowledge of factors influencing the nature, causation, and prevention of ill health. Her approach to these yet unsolved problems is based on healthy appreciation of the present status of mental hygiene and she clearly depicts the situation thus: "From the standpoint of pure science, mental hygiene is hardly out of its swaddling clothes and many more decades of research and experimentation will be necessary before such a happy consummation will be achieved. The evolution of every science and art has been a slow fumbling and stumbling toward the light of truth; and mental hygiene is no exception to this rule. The only development possible is through the conscientious application of the best knowledge available at the moment, followed by a keenly critical appraisal of the accumulated experience and results obtained, which in turn brings about modifications in theory and practice so that these are ever more closely in accord with the facts and needs of the situation. Through this process mental hygiene will gradually emerge from the haze of conflict which envelops the various schools of thought, its theories will be more precisely defined, clarified, consolidated and tested and a more and more effective instrument for the study, treatment and prevention of mental and behavior disorders will be forged."

The book, comprising twelve chapters with index and list of bibliographies, lends itself to convenient assignments in reading courses or text study. The first chapter consists of introduction to the subject; the second a discussion of medicine with special reference to the recognition that every form of illness has a psychic component, and to the need for graduate and undergraduate instruction. The third chapter discusses the position of nursing in the field; the fourth the place of social service agencies, followed by other chapters devoted to the subjects of delinquency and law, parental education, the pre-school child, education and teacher training, the church and theological training, industry, recreation, and psychiatric institutions and agencies.

W. L. T.

*The Lyophilic Colloids (Their Theory and Practice).* By MARTIN H. FISCHER, Professor of Physiology in the University of Cincinnati, and MARIAN O. HOOKER, Research Associate in Physiology in the University of Cincinnati. Ed. I. iiii + 246 pages; 16 x 25 cm. Charles C. Thomas, Springfield, Ill. 1933 Price, $4.50.

The increasing importance of colloid chemistry in the field of experimental physiology bespeaks the timely nature of a treatise of this kind from the pen of the first author and his associate. This book summarizes the investigations of the authors in colloid chemistry which have extended over a period of fifteen years.

The book is divided into three parts. Part one deals with the "General Nature of the Lyophilic Colloid"; part two, points out the "Chemical Applications" and part three considers the "Biological Applications."

The subject matter of part one consists of a description of the physical and chemical properties of various lyophilic colloid systems, such as phenol water, gelatin water and casein water. Many tables and photographs are included to illustrate the subject matter under discussion. The theoretical aspects of the subject are most interestingly treated by the authors.

Part three is of special interest to the readers of this journal. The osmotic concept of the living cell is critically examined. Edema is discussed as a problem in colloid chemistry along with several very important practical suggestions on acidosis and alkalosis. The authors warn against persistence in attempting to show that the

physicochemical laws of dilute solutions apply to biological phenomena. They prefer considering these solutions in cells as "solutions of the inverse type." They state: "When we have discovered their laws, when we have familiarized ourselves with the physicochemical and colloid-chemical behavior of systems of the type water-dissolved-in-*x*, we shall find ourselves possessed also of the laws which govern the behavior of protoplasm under physiological and pathological circumstances."

J. C. K., JR.

*Diet and Personality. Fitting Food to Type and Environment.* By L. JEAN BOGERT, Ph.D.; with an introduction by LAFAYETTE B. MENDEL, Ph.D., Sc.D., Sterling Professor of Physiological Chemistry, Yale University. ix + 223 pages; 14 x 20 cm. Macmillan Co., New York. 1934. Price, $2.00.

This is a book giving popular medical advice, written by a non-medical author. The advice is not confined to diet alone, but includes many topics, such as a discussion of exercise, rest, fresh air, sunshine, nervous strain, smoking, bathing, posture, hours of sleep, and care of the teeth and bowels. It is written in the chatty, semi-facetious style which has had so great a vogue among books of this character during the past few years. There is nothing that is new or original in this book, or that has not been better done in a number of its predecessors.

G. A. H.

# PROGRAM
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(*e*) House Officers of the hospitals participating in the program, upon presentation of proper identification.

(*f*) Members of the Medical Corps of the Public Services of the United States and Canada, without registration fee, upon presentation of proper credentials.

(*g*) Qualified physicians who may wish to attend this Session as visitors. Such physicians shall pay a registration fee of $12.00, and shall be entitled to one year's subscription to the ANNALS OF INTERNAL MEDICINE (in which the proceedings will be published), included within such fee.

REGISTRATION BUREAU.—Located at the entrance to the Exhibit Room on the Fourth Floor of the Palmer House. Hours: 8:30 a.m. to 6:00 p.m., daily, April 16–20.

REGISTRATION BLANKS FOR ALL CLINICS AND DEMONSTRATIONS will be sent with the program to members of the College. Guests will secure registration blanks at the Registration Bureau during the Session.

TRANSPORTATION.—Round trip tickets will be available on the basis of one and one-third of the current one-way first-class fares, with minimum excursion fare of $1.00 for the round trip, upon presentation of identification certificates to be procured from the Executive Secretary of the American College of Physicians. The reduced fares will apply for physicians and dependent members of their families.

Members are privileged to make the going journey by one route and return by another route. Stop-overs will be allowed at all stations within final limit on either going or return trip, or both, upon application to conductors.

*Before purchasing tickets, members must secure from the Executive Secretary an Identification Certificate, to entitle them to the reduced fares.*

In general, tickets will be sold from April 10 to April 18, depending upon the relative distance from Chicago, with a return limit of thirty days in addition to date of sale.

*All tickets must be validated by a special railroad agent at the Chicago Headquarters from April 16 to 20.*

THE GENERAL BUSINESS MEETING OF THE COLLEGE will be held at 5:00 p.m., Thursday, April 19, immediately following the general scientific program of the afternoon. All Masters and Fellows of the College are urged to be present.

There will be the election of Officers, Regents and Governors, the reports of the Treasurer and of the Executive Secretary, and the induction to office of the new President, Dr. Jonathan C. Meakins, Montreal, Que.

## SPECIAL FEATURES

### Monday, April 16, 1934

THE ANNUAL SMOKER.—Immediately following the scientific program, at about 10:20 o'clock, Monday evening, in the Red Lacquer Room of the Palmer House. An unusual program of entertainment, both amusing and instructive, will be presented.

Wednesday, April 18, 1934

CONVOCATION OF THE COLLEGE.—8:00 o'clock, Grand Ballroom, Palmer House. All Masters and Fellows of the College and those to be received in Fellowship should be present. Newly elected Fellows who have not yet been received in Fellowship are requested to occupy the central section of seats especially reserved for them. As this is the most formal meeting of the College, it is suggested that all appear in evening dress.

The Convocation is open to all physicians and their families generally, and to such of the general public as may be interested.

Following the Convocation Ceremony, the President of the College will deliver the annual Presidential address to the Masters, Fellows and Associates. Dr. Grant Fleming, Director of the Department of Public Health and Preventive Medicine, McGill University, Montreal, will deliver an address on "The Medical Aspects of National Health Insurance."

The Presidential Reception will follow immediately after the program. Newly inducted Fellows should sign the Roster and secure their Fellowship Certificates during the interim between the Convocation and the Reception. Dancing in the Red Lacquer Room.

THE EXPOSITION AND COMMERCIAL EXHIBIT will be located in the Exhibit Hall of the Palmer House.

Exhibits consisting of medical literature and texts, pharmaceutical products, apparatus and appliances, special foods, etc., will be shown by leading publishers and manufacturers. These exhibits afford an opportunity for physicians to examine the latest literature and the newest products in the field of medicine generally; their educational value should not be overlooked. Every attendant at the Session is urged to visit each of the booths, for he cannot help but find something new, interesting and scientifically valuable. Intermissions in the general program have been arranged from Tuesday to Friday, inclusive, for the purpose of providing a definite time for the inspection of exhibits.

## COMMERCIAL EXHIBITORS

*(The following is a partial list of exhibitors who have engaged space at the Eighteenth Annual Clinical Session of the American College of Physicians, Chicago, Ill.)*

| | *Space* |
|---|---|
| Abbott Laboratories, North Chicago, Ill. | 51 |
| American Agency of French Vichy, Inc., New York, N. Y. | 55 |
| Appleton-Century Company, D., New York, N. Y. | 68 |
| Ayerst, McKenna & Harrison, Limited, Montreal, Que. | 16 |
| Battle Creek Food Company, The, Battle Creek, Mich. | 13 |
| Becton, Dickinson & Co., Rutherford, N. J. | 62 |
| Betz Company, Frank S., Hammond, Ind. | 20 |
| Bilhuber-Knoll Corp., Jersey City, N. J. | 60 |
| Burdick Corporation, The, Milton, Wis. | 36–37 |
| Cambridge Instrument Co. Inc., New York, N. Y. | 56 |
| Cameron Surgical Specialty Co., Chicago, Ill. | 18 |
| Chappel Bros. Inc., Rockford, Ill. | 22 |
| Chicago Dietetic Supply House Inc., The, Chicago, Ill. | 28 |
| Collins, Inc., Warren E., Boston, Mass. | 9 |
| Corn Products Refining Co., New York, N. Y. | 17 |
| Davies, Rose & Co., Ltd., Boston, Mass. | 50 |
| Davis Company, F. A., Philadelphia, Pa. | 4 |

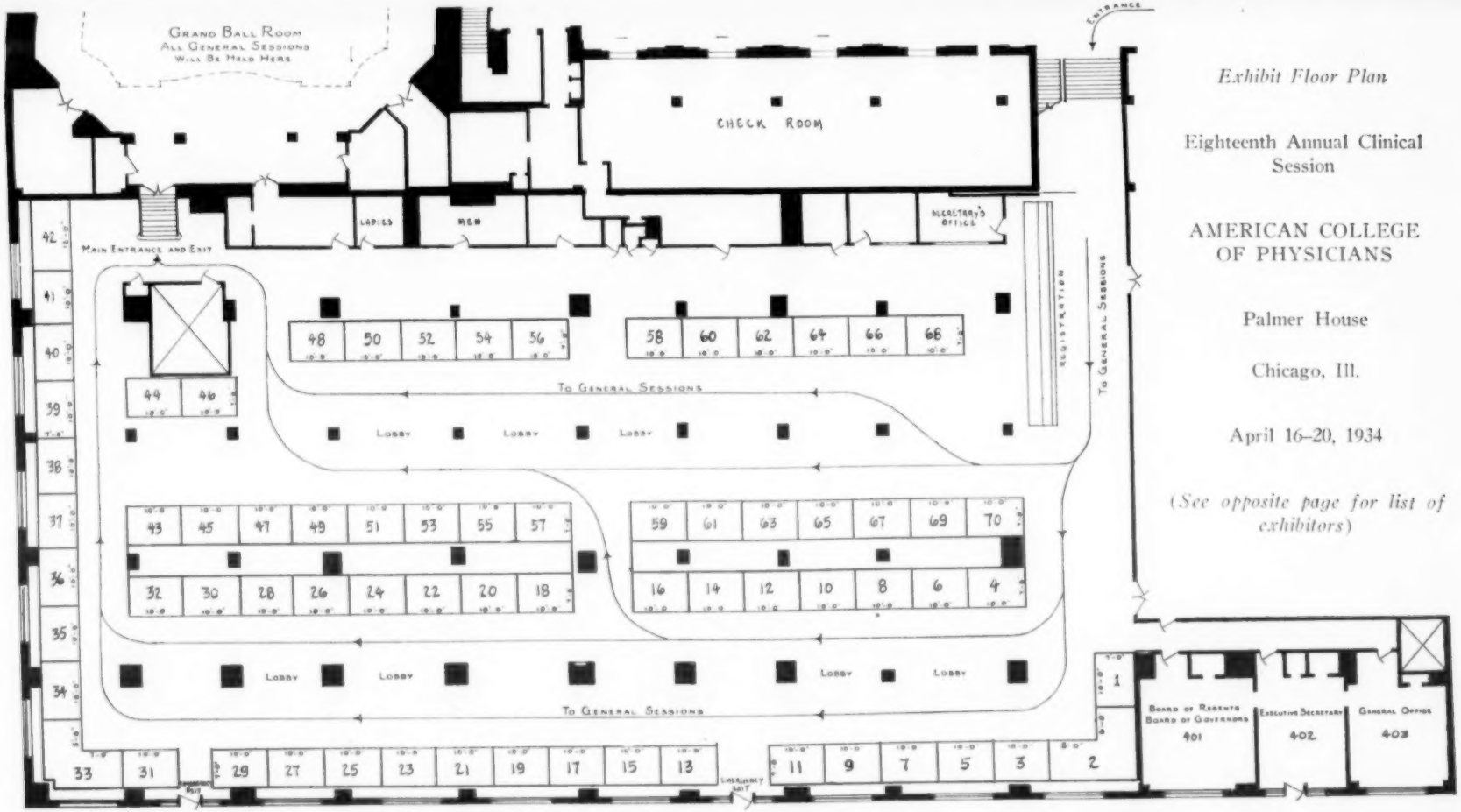


*Exhibit Floor Plan*

Eighteenth Annual Clinical Session

AMERICAN COLLEGE OF PHYSICIANS

Palmer House

Chicago, Ill.

April 16–20, 1934

*(See opposite page for list of exhibitors)*

Davis Company, R. B., Hoboken, N. J. ..... 53
Doak Company, The, Cleveland, Ohio ..... 57
Fougera and Co. Inc., E., New York, N. Y. ..... 8
General Electric X-Ray Corporation, Chicago, Ill. ..... 1–2–3–5
General Mills Inc., Minneapolis, Minn. ..... 31
Gerber Products Company, Fremont, Mich. ..... 42
Gradwohl School of Laboratory Technique, St. Louis, Mo. ..... 61
Hamilton Manufacturing Co., Two Rivers, Wis. ..... 34–35
Health Products Corporation, Newark, N. J. ..... 65
Hynson, Westcott & Dunning, Inc., Baltimore, Md. ..... 14
Kalak Water Co. of New York, Inc., New York, N. Y. ..... 32
Kellogg Company, Battle Creek, Mich. ..... 45
LaMotte Chemical Products Company, Baltimore, Md. ..... 58
Lea & Febiger, Philadelphia, Pa. ..... 52
Lederle Laboratories Inc., New York, N. Y. ..... 38
Lippincott Company, J. B., Philadelphia, Pa. ..... 69
Login Brothers, Chicago, Ill. ..... 19
M & R Dietetic Labs., Inc., Columbus, Ohio ..... 63
Macmillan Company, The, New York, N. Y. ..... 70
Maltine Company, The, New York, N. Y. ..... 48
Mead Johnson & Co., Evansville, Ind. ..... 33
Medical Bureau, The, Chicago, Ill. ..... 7
Medical Case History Bureau, New York, N. Y. ..... 43
Merck & Co. Inc., Rahway, N. J. ..... 64–66
Metz Laboratories, Inc., H. A., New York, N. Y. ..... 41
Merrell Company, The Wm. S., Cincinnati, Ohio ..... 30–44
Middlewest Instrument Company, Chicago, Ill. ..... 39
Mosby Company, The C. V., St. Louis, Mo. ..... 12
Petrolagar Laboratories, Inc., Chicago, Ill. ..... 67
Phillips Chemical Co., The Chas. H., New York, N. Y. ..... 47
Sanborn Company, Cambridge, Mass. ..... 46
Sandoz Chemical Works, Inc., New York, N. Y. ..... 10
Saunders Company, W. B., Philadelphia, Pa. ..... 54
Schering Corporation, Bloomfield, N. J. ..... 26
Searle & Co., G. D., Chicago, Ill. ..... 6
Squibb & Sons, E. R., New York, N. Y. ..... 49
Stearns & Company, Frederick, Detroit, Mich. ..... 11
Sun-A-Sured, Inc., Chicago, Ill. ..... 24
Upsher Smith Company, Minneapolis, Minn. ..... 15
Wander Co., The, Chicago, Ill. ..... 59
Winthrop Chemical Company, Inc., New York, N. Y. ..... 41

## CHICAGO PROGRAM OF ENTERTAINMENT FOR VISITING WOMEN

A program of special features has been arranged, but ample time has been allowed for sight-seeing, shopping and recreation. Complete lists of museums, principal shops, current public lectures, concerts, and theaters will be issued by the local committee.

### MONDAY, APRIL 16, 1934

*Morning:* Registration at the Palmer House—9 a.m. to 5 p.m.

Suggestions: The Art Institute, The Field Museum of Natural History, The Adler Planetarium, and the Shedd Aquarium.

TUESDAY, APRIL 17, 1934

*Morning:* Registration at the Palmer House—9 a.m. to 5 p.m.

*Afternoon:* The visiting women will be the guests of the local committee at a reception and luncheon at the Casino Club, 195 East Delaware Place, at twelve-thirty.

This makes a convenient starting point for visits to the Alexander McKinlock Campus of Northwestern University, to Lincoln Park in which are located the Museum of the Chicago Academy of Sciences, the famous St. Gauden's statue of Lincoln, the beautiful new building of the Chicago Historical Society and other points of interest. The drive along Lake Michigan through Lincoln Park over newly made land to Foster Avenue and return is most attractive and affords one of the finest views of Chicago's sky line. The Casino Club is a block east of upper Michigan Avenue which is famous for its shops.

WEDNESDAY, APRIL 18, 1934

*Afternoon:* The members of the local committee invite the visiting women to a tea at the Arts Club, 410 North Michigan Avenue (Wrigley Building North) from four-thirty to six.

*Evening:* The Convocation of the College is held in the Grand Ballroom of the Palmer House at eight o'clock. The women are invited to attend.

THURSDAY, APRIL 19, 1934

*Morning:* 10:00 o'clock. Special busses will leave the Palmer House for the University of Chicago Campus where visits will be made to the Oriental Institute and the International House. Those who wish to visit the Museum of Science and Industry located in the Fine Arts Building of the 1893 World's Fair which has been reconstructed in marble, may obtain luncheon at the International House.

*Evening:* 7:30 o'clock. The Annual Banquet of the College at the Palmer House.

## GENERAL SESSIONS

The membership of the American College of Physicians is composed of internists who represent every branch and subdivision of internal medicine. This fact has been borne in mind in the preparation of the program for the General Sessions. An effort has been made to present timely subjects that will prove not only of interest to medical men in general, but will also be of definite value to those engaged in the more special fields of medicine. The speakers, who come from various parts of this country and Canada, have been selected because of their fitness to speak with authority upon the subjects in which they are particularly interested. We have endeavored to stress on this program topics in which widespread interest has developed or in which definite advances have been made recently. The limited time available for the General Sessions has made it obviously impossible to include all the subjects of importance to the internist, but it is earnestly hoped that the choice that has been made will furnish a program that will prove both interesting and profitable.

Special attention should be called to certain features of the program.

*Cardiovascular Disease* which is constantly attaining increased importance in our modern civilization will accordingly be especially emphasized. A number of papers will be found devoted to various practical considerations of this subject. Notable among these are the contributions on coronary occlusion, a discussion of the most recent observations on the etiology of arterial hypertension, and papers dealing with

the rôle of total ablation of the thyroid in angina pectoris and congestive heart failure and the use of a new drug in cardiovascular disease. Great interest has been shown of late in the diagnosis and treatment of peripheral vascular disease. This subject will be discussed by one of the outstanding workers in this field.

*Infectious Diseases* have been accorded definite consideration. Among the important topics to be discussed are a recent encephalitis epidemic, certain virus diseases transmissible to man, undulant fever, the permanent nature of various acute infections, and the latest advance in the treatment of lobar pneumonia; namely, therapeutic pneumothorax.

*Metabolic Diseases* have not been neglected. Certain aspects of diabetes will be considered, as well as subjects of such wide physiological and clinical interest as energy exchange in disease and alkalosis.

*Nervous Diseases* will be discussed chiefly from the viewpoint of the internist. The psychological approach to the patient will be stressed, as well as certain problems in organic neurology and fever therapy.

*Hematology*—Although, because of its recent and admirable presentation before the College, the subject of pernicious anemia will not be discussed, other important aspects of diseases of the blood will be considered. There will be an essay on the broad subject of development in blood studies. Various aspects of granulopenia, newer conceptions of the monocyte, and the practical value of blood sedimentation tests will be considered.

*Gastro-enterology* will be covered from certain special angles. The recent advances in the physiology of the liver and biliary tract and the value of estimating the functional capacity of the liver will be emphasized. Various intestinal conditions and their management, as well as the relationship between gastrointestinal and other visceral diseases, will be considered.

*Tuberculosis* will be given adequate consideration, especially from the standpoint of its medical and surgical treatment. There will be a paper on the newer conception of hematogenous pulmonary tuberculosis, as well as one on cutaneous tuberculosis.

*Pulmonary Diseases* will be discussed from the standpoint of the bronchoscopist, and special topics such as lung abscess and bronchomoniliasis will also be discussed.

*Pediatrics*—An effort has been made to have a number of outstanding contributions presented dealing with some of the broad problems that are engaging the attention of those who are particularly interested in internal medicine as it applies to children.

A number of other important but unrelated subjects will be discussed during the General Sessions. For example, papers will be presented on the relationship of allergic diseases to internal medicine, as well as on the new group of drugs known as metabolic stimulants; diaphragmatic hernia; studies on the etiology of cancer; physical therapy; certain aspects of rheumatoid arthritis, and other papers of equal importance.

Endocrinology, which was so completely covered at the last meeting of the College, will not have a prominent part in the program this year.

The much discussed topic of *national health insurance* will be the subject of an address by a distinguished speaker who is unusually well qualified to discuss this timely problem.

It has been possible to construct a program such as the one above outlined, which we trust will prove a well-balanced grouping of papers on subjects of outstanding importance, because of the hearty coöperation and ready response of the Fellows of the College and the others who were invited to participate in the General Sessions. To all of them are due our sincere thanks.

## GENERAL SESSIONS

Chicago, Ill.—April 16–20, 1934

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### OPENING GENERAL SESSION

Monday Afternoon, April 16, 1934

2:00 o'Clock

GRAND BALLROOM, PALMER HOUSE

1. Addresses of Welcome:
   James B. Herrick, General Chairman of the Eighteenth Annual Clinical Session.
   Austin A. Hayden, President of the Chicago Medical Society.
   Irving S. Cutter, On Behalf of the Chicago Medical Schools.
2. Response to Addresses of Welcome:
   George Morris Piersol, President of the American College of Physicians.
3. Arteriolar Infarction.
   Jonathan C. Meakins, Montreal, Que.
4. Malaria Therapy in Asymptomatic Neurosyphilis.
   Paul A. O'Leary, Rochester, Minn.
5. Bronchoscopy in Pulmonary Disease: Its Present Status as an Aid in Diagnosis and Treatment.
   Gabriel Tucker, Philadelphia, Pa.
6. Diaphragmatic Hernia.
   Carl A. Hedblom, Chicago, Ill.
7. Observations on the Diagnosis and Treatment of Peripheral Vascular Disease.
   Eugene M. Landis, Philadelphia, Pa.
8. Hepatic Function in Relation to Hepatic Pathology.
   Frank C. Mann, Rochester, Minn.

### SECOND GENERAL SESSION

Monday Evening, April 16, 1934

8:00 o'Clock

GRAND BALLROOM, PALMER HOUSE

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Presiding Officer
James Alex. Miller, New York, N. Y.

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1. Development and Disappointments in Blood Studies.
   Roger I. Lee, Boston, Mass.
2. The Tuberculosis of Childhood.
   Charles Hendee Smith, New York, N. Y.
3. The Permanent Nature of Various Common Infections.
   Allen K. Krause, Tucson, Ariz.
4. Therapeutic Pneumothorax in Experimental Lobar Pneumonia in Dogs.
   Simon S. Leopold, Philadelphia, Pa.

5. Virus Diseases of Animals Transmissible to Man.
Karl F. Meyer, San Francisco, Calif.

10:20 o'Clock

SMOKER

Red Lacquer Room, Palmer House

An unusual program of entertainment, both amusing and instructive, has been arranged.

THIRD GENERAL SESSION

Tuesday Afternoon, April 17, 1934

2:00 o'Clock

GRAND BALLROOM, PALMER HOUSE

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Presiding Officer
Ernest B. Bradley, Lexington, Ky.

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1. Energy Exchange in the Study and Management of Disease.
L. H. Newburgh, Ann Arbor, Mich.
2. Leukopenia in Tuberculosis with Report of a Case Showing a Complete Neutropenic Episode for One Week,—Recovery.
Charles H. Cocke, Asheville, N. C.
3. Newer Clinicopathologic Considerations of the Monocyte and of Monocytic Leukosis.
Charles A. Doan and Bruce K. Wiseman, Columbus, Ohio.
4. The Diagnosis and Management of Certain Types of Chronic Diarrhea.
Philip W. Brown, Rochester, Minn.
5. Small Intestinal Intubation: Experiences with a Double-Lumened Tube.
T. Grier Miller and W. Osler Abbott, Philadelphia, Pa.
6. The Criteria of Alcohol Intoxication with Special Reference to 3.2 Beer.
A. J. Carlson, Chicago, Ill.

INTERMISSION

7. Proliferative and Exudative Tuberculosis in Their Relationship to the Various Fractions of the Tubercle Bacillus.
Francis M. Pottenger, Monrovia, Calif.
8. Metabolic Stimulants (Sodium Dinitrophenol).
Edward L. Bortz, Philadelphia, Pa.
9. Surgical Treatment of Pulmonary Tuberculosis.
Ralph C. Matson, Portland, Ore.
10. Allergic Diseases in General Practice.
Harry B. Wilmer and Merle Miller, Philadelphia, Pa.
11. Institutional Treatment for the Chronic Invalid and Convalescent.
Elmer L. Eggleston, Battle Creek, Mich.

## FOURTH GENERAL SESSION

Tuesday Evening, April 17, 1934

8:00 o'Clock

GRAND BALLROOM, PALMER HOUSE

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Presiding Officer
Arthur R. Elliott, Chicago, Ill.

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1. The Encephalitis Epidemic in St. Louis.
   David P. Barr, St. Louis, Mo.
2. Results of Further Studies on the Physiology of the Anterior Pituitary.
   J. B. Collip, Montreal, Que.
3. Treatment of Angina Pectoris and Congestive Heart Failure by Total Ablation of the Thyroid in Patients without Thyrotoxicosis.
   Herrman L. Blumgart, Boston, Mass.
4. Studies of Cell Potencies and Some Relations to Neoplasia.
   Stanley P. Reimann, Philadelphia.
5. Biliary Dyskinesia.
   A. C. Ivy, Chicago, Ill.
6. Hematogenous Pulmonary Tuberculosis.
   James Alex. Miller, New York, N. Y.

## FIFTH GENERAL SESSION

Wednesday Afternoon, April 18, 1934

2:00 o'Clock

GRAND BALLROOM, PALMER HOUSE

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Presiding Officer
James G. Carr, Chicago, Ill.

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1. The Recent Trend Towards a Differentiation between Allergy and Immunology, and the Relationship to Clinical Medicine.
   Lay Martin, Baltimore, Md.
2. An Explanation of the Mechanism of Infantile Paralysis Production in the Human.
   John A. Toomey, Cleveland, Ohio.
3. A Critical Discussion of the Etiological Factors in Arterial Hypertension.
   Soma Weiss, Boston, Mass.
4. Remarks on the Diagnosis of Coronary Occlusion.
   Louis Hamman, Baltimore, Md.
5. Cutaneous Tuberculosis and Its Relationship to General Medicine.
   Francis E. Senear, Chicago, Ill.

INTERMISSION

6. The Blood Sedimentation Test: The Value of Its Use as a Routine, Especially in Pulmonary Tuberculosis.
   Paul H. Ringer, Asheville, N. C.

7. Glycogen Formation in Diabetes.
   F. D. W. Lukens, Philadelphia, Pa.
8. Trends in Diet in Diabetes.
   R. T. Woodyatt, Chicago, Ill.
9. The Diabetic Child.
   Henry J. John, Cleveland, Ohio.
10. Alkalosis: A Clinical Problem.
    Charles T. Way and Edward Muntwyler, Cleveland, Ohio.
11. Certain Bases of Physical Therapy.
    Thomas P. Sprunt, Baltimore, Md.
12. Acquired Heart Block with Adams-Stokes Attacks Dependent upon a Congenital Anomaly (Persistent Ostium Primum): Report of a Case.
    Wallace M. Yater, Washington, D. C., Chas. W. Barrier, Fort Worth, Tex., and Paul E. McNabb, Washington, D. C.

## ANNUAL CONVOCATION

Wednesday Evening, April 18, 1934

8:00 o'Clock

GRAND BALLROOM, PALMER HOUSE

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The general profession and the general public are cordially invited. No special admission tickets are required.

1. Convocation Ceremony.
2. Address: "The Medical Aspects of National Health Insurance."
   Grant Fleming, Director of the Department of Public Health and Preventive Medicine, McGill University, Montreal, Que.
3. Presidential Address.
   George Morris Piersol, Philadelphia, Pa.

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Presidential Reception

RED LACQUER ROOM

The Reception will follow immediately after the program. Newly inducted Fellows should sign the Roster and secure their Fellowship Certificates during the interim between the Convocation and the Reception.

Dancing

## SIXTH GENERAL SESSION

Thursday Afternoon, April 19, 1934

2:00 o'Clock

GRAND BALLROOM, PALMER HOUSE

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Presiding Officer
Jonathan C. Meakins, Montreal, Que.

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1. Further Studies on Granulopenia with Report of Fifteen Additional Cases.
   Stewart R. Roberts and Roy R. Kracke, Atlanta, Ga.

2. Non-Painful Features of Coronary Occlusion.
S. Marx White, Minneapolis, Minn.
3. Classification of Vascular Disease with Special Reference to Etiology, Pathological Anatomy and Pathological Physiology.
Nathan S. Davis, III, Chicago, Ill.
4. Blood Pressure Variations as a Guide to Treatment and Prognosis.
Clarence L. Andrews, Atlantic City, N. J.
5. The Early Recognition of Myocardial Disease.
Walter L. Bierring, Des Moines, Iowa.
6. The Use of Verodigen (a Digitalis Glucoside) in Cardiovascular Disease: Its Pharmacological Assay and Effects on Animals.
W. D. Stroud, A. E. Livingston, A. W. Bromer, J. B. Vander Veer and G. C. Griffith, Philadelphia, Pa.

INTERMISSION

7. Cardiovascular Observations in 215 Neurosyphilitics.
Clough T. Burnett and Charles A. Rymer, Denver, Colo.
8. Influential Factors in Recovery from Rheumatoid Arthritis.
Russell L. Cecil, New York, N. Y.
9. Creatine Metabolism and Blood Cholesterol as Aids in the Diagnosis and Treatment of Hypothyroidism in Children.
Julius H. Hess, Chicago, Ill.

*The Annual General Business Meeting* of the College will be held in the *Red Lacquer Room* immediately after the last paper. All Masters and Fellows are urged to attend. Official reports from the Executive Secretary and Treasurer will be read; new Officers, Regents and Governors will be elected, and the President-Elect, Dr. Jonathan C. Meakins, will be inducted into office.

Thursday Evening, 8:00 o'Clock

GRAND BALLROOM, PALMER HOUSE

THE ANNUAL BANQUET OF THE COLLEGE

(Procure Tickets at the Registration Bureau)

Toastmaster: James B. Herrick, Chicago, Ill.
Address: "The Renewal of America."
Dr. Glenn Frank, President of the University of Wisconsin.

FINAL GENERAL SESSION

Friday Afternoon, April 20, 1934

2:00 o'Clock

GRAND BALLROOM, PALMER HOUSE

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Presiding Officer
James H. Means, Boston, Mass.

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1. The United States Pharmacopoeia XI. Its Relation to Internal Medicine and the Scientific Nature of Its Revision.
Virgil E. Simpson, Louisville, Ky.

2. The Treatment of Lung Abscess.
   Frederick T. Lord, Boston, Mass.
3. Evaluation of Methods for Testing the Functional Capacity of the Liver.
   William J. Kerr, San Francisco, Calif.
4. Abdominal Pain: Its Significance and Diagnostic Value.
   Thomas R. Brown, Baltimore, Md.
5. Diseases of the Nervous System Producing Dysfunction of other Organs, and Dysfunction of other Organs Producing or Simulating Diseases of the Nervous System.
   Lewis J. Pollock, Chicago, Ill.
6. The Thymus and Status Thymico-Lymphaticus.
   A. Graeme Mitchell, Cincinnati, Ohio.

INTERMISSION

7. Undulant Fever.
   Joseph L. Miller, Chicago, Ill.
8. Personality Study in the Practice of Internal Medicine.
   Edward Weiss, Philadelphia, Pa.
9. A Study of Ten Cases of Bronchomoniliasis.
   John W. Flinn, Robert S. Flinn and Zebud M. Flinn, Prescott, Ariz.
10. Factors Influencing Operative Mortality in Hyperthyroidism.
    Willard O. Thompson, S. G. Taylor, III, and Karl A. Meyer, Chicago, Ill.
11. The Interrelationship of Renal and Gastrointestinal Disease.
    Harry Gauss, Denver, Colo.

## THE CLINIC PROGRAM

An effort has been made in preparing the program to render available what is most interesting in medicine that Chicago has to offer. The laboratories and clinical centers of the Universities have been enlisted to display the best they have in research and clinic, while the Cook County Graduate School of Medicine, in affiliation with Cook County Hospital, will furnish unusual facilities to survey the work being done in that great hospital.

A special effort has been made to include in the program a larger contribution from Pediatrics than is usual. Roentgenology has been drawn upon heavily and interesting demonstrations in tuberculosis have been arranged for. Clinico-pathologic conferences, symposia on endocrinology, cardiovascular problems, neurology, and hematology, besides mixed clinics of varied interest, will be given in the principal hospitals.

Convenience of access has been kept in view and the geographic area covered is sufficiently circumscribed to avoid waste of time in getting from one center to another.

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Clinics and demonstrations will be held in the forenoons from 9:00 to 12:00 daily, Tuesday to Friday, inclusive.

*Tickets will be required for each and every one of the special clinics, ward rounds and demonstrations.* The coöperation of every one in securing his clinic tickets will assist greatly in distributing the attendance according to the capacity of each program. It is self-evident that a ward round arranged for twenty-five will lose its value for all if forty or fifty are present. Ticket registration naturally is the only effective method of keeping the attendance within the capacities indicated.

Tuesday, April 17, 1934

A-1 UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Room P 117

(Capacity—256)

9:00– 9:20 Experimental Studies on the Etiology of Peptic Ulcer.
Warren B. Matthews.

9:20– 9:40 The Relative Importance of Acid and of Pepsin in the Etiology of Ulcer.
Lester R. Dragstedt.

9:40–10:00 The Treatment of Peptic Ulcer.
Walter L. Palmer.

10:00–10:45 The Relationship of Circulating Antipneumococcal Immune Substances to the Course of Lobar Pneumonia.
O. H. Robertson, J. B. Graeser and L. T. Coggeshall.

10:45–11:30 The Diagnosis of Early Pulmonary Tuberculosis.
Robert G. Bloch.

11:30–12:00 Experimental Poliomyelitis.
N. Paul Hudson.

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A-2 UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Room M 137

(Capacity—85)

9:00– 9:30 Motion Pictures of Experimental Increased Intracranial Pressure.
Arno B. Luckhardt.

9:30–10:00 Clinical Aspects of Increased Intracranial Pressure.
Paul C. Bucy.

10:00–10:30 Peculiarities of Intracranial Tumors in Childhood.
Percival Bailey.

10:30–11:15 Some Recent Observations on the Physiology of Sleep.
Nathaniel Kleitman.

11:15–11:30. Pain.
Arno B. Luckhardt.

11:30–12:00 Studies on the Physiology of the Bladder with Operative Relief of Vesical Paralysis.
Douglas N. Buchanan and Charles B. Huggins.

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A-3 UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Room M 433

(Capacity—25)

9:00–10:30 Bedside Clinic on Cardiac and Renal Vascular Diseases.
Louis Leiter and Emmet B. Bay.

A-4 UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Outside of Room P 118

(No set capacity)

9:00–12:00 The Rôle of X-Ray in the Clinical Study of Heart Disease—Exhibition of Films.
Paul C. Hodges.

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B CHILDREN'S MEMORIAL HOSPITAL
(700 Fullerton Avenue)

Auditorium, Nurses' Home

(Capacity—250)

Dr. Brennemann will discuss each subject briefly by way of introduction. The main presentation will be of x-ray lantern slides.

9:00–10:00 Empyema in Children with Special Emphasis on the Rôle of Aspiration in Treatment.
E. T. McEnery.

10:00–11:00 X-Ray Diagnosis of Intrathoracic Tuberculosis in Children.
J. A. Bigler.

11:00–12:00 The Interrelationship of Collapsed Lung, the Triangular X-Ray Lung Shadow and Bronchiectasis.
W. E. Anspach.

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C-1 COOK COUNTY GRADUATE SCHOOL OF MEDICINE
(In affiliation with the Cook County Hospital)
COOK COUNTY HOSPITAL
(West Harrison and South Wood Streets)

Medical Amphitheatre

(Capacity—150)

9:00– 9:45 Amebiasis and Its Therapy.
Sidney A. Portis.

9:45–10:30 Gastric and Duodenal Ulcer.
Jacob Meyer.

10:30–11:15 Diabetes and Cardiovascular Disease.
William J. Quigley.

11:15–12:00 Atypical Types of Perforated Peptic Ulcer.
Harry Singer.

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C-2 COOK COUNTY GRADUATE SCHOOL OF MEDICINE
(West Harrison and South Wood Streets)

Surgical Amphitheatre

(Capacity—150)

9:00–9:45 Pulmonary Heart Disease.
Harry J. Isaacs.

9:45–10:30 Rheumatic Diseases.
Isadore Pilot.
10:30–11:15 Pituitary Disorders.
Frank B. Lusk.
11:15–12:00 Presentation of Heart Cases.
Laurence E. Hines.

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C-3 COOK COUNTY GRADUATE SCHOOL OF MEDICINE
(West Harrison and South Wood Streets)

Amphitheatre—Children's Building

(Capacity—100)

9:00– 9:45 Rheumatic Heart Disease in Children.
Philip Rosenblum.
9:45–10:30 Tremor in Newly Born.
Maxwell P. Borovsky.
10:30–11:15 Pulmonary Disease in Children.
Maurice L. Blatt.
11:15–12:00 Diagnosis and Treatment of Gonorrheal Vaginitis.
Maurice Schneider.

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C-4 COOK COUNTY GRADUATE SCHOOL OF MEDICINE
(West Harrison and South Wood Streets)

Bedside Clinics

(Capacity—15)

C-4a 9:00–11:00 Ward 64.
Harry J. Isaacs.
C-4b 10:00–12:00 Ward 54.
Jacob Meyer.
C-4c 10:30–12:00 Ward 64.
Italo F. Volini.
C-4d 11:00–12:00 Ward 61.
Frederick Tice.

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D UNIVERSITY OF ILLINOIS
(1817 W. Polk Street)

Room 106

(Capacity—200)

R. W. Keeton presiding

9:00– 9:20 The Clinical Differentiation of Medical and Surgical Jaundice.
Edmund F. Foley.
9:20– 9:40 Syphilis of the Stomach.
Harry A. Singer.
9:40–10:00 The Management of Ulcerating Diseases of the Colon.
Michael H. Streicher.
10:00–10:20 The Physiology of the Failing Heart.
M. B. Visscher.

10:20–10:40 Long Standing Valvular Disease: Onset of Auricular Fibrillation without Effect upon Benign Course of the Disease.
Sidney Strauss.

10:40–11:00 Neuro-circulatory Asthenia: An Attempt to Analyze the Mechanism Involved.
Ford K. Hick.

11:00–11:20 The Differentiation of Hemophilia from Purpura Hemorrhagica and Other Hemorrhagic Disease with Blood. (Lantern slide demonstration.)
Carroll L. Birch.

11:20–11:40 Dental Extractions in Hemophiliacs.
Walter W. Dalitsch.

11:40–12:00 Arthritis Classification and Therapy with Particular Reference to the Use of Vaccine.
Isadore Pilot.

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E

## LOYOLA UNIVERSITY and MERCY HOSPITAL
(2537 Prairie Avenue)

Amphitheatre

(Capacity—350)

9:00–10:00 Endocrine Clinic.
A. W. Schram.

10:00–11:00 Gastrointestinal Clinic.
Fred M. Drennan.

11:00–12:00 Cardiorenal Clinic.
Milton Mandel.

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F-1

## MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Sarah Morris Amphitheatre, 2901 Ellis Avenue

(Capacity—170)

*Gallbladder Study Group*

9:00– 9:15 Discussion of Recent Investigative Work in Gallbladder Disease.
Leon Bloch.

9:15– 9:30 Preoperative and Postoperative Medical Care of Gallbladder Patients.
Sidney A. Portis.

9:30– 9:40 Bromsulphonphthalein Liver Function Test: Crystalography as Aid in Diagnosis of Lithiasis.
A. Serby.

9:40– 9:50 The Galactose and Urobilinogen Tests in the Differential Diagnosis of Jaundice.
D. Rosenberg.

9:50–10:00 Electrocardiographic Tracings During Manipulations of Gallbladder at Operation.
L. Katz.

10:00–10:10 The Liver in Gallbladder Disease.
S. Soskin.

10:10–10:20 Correlation of X-Ray and Pathological Findings in a Series of Patients Operated Upon for Gallbladder Disease.
G. Lichtenstein.

10:20–10:40 Gallbladder Disease and Surgery. A Report of Methods of Diagnosis, Treatment and Especially Results.
Ralph B. Bettman.
10:40–11:00 Discussion: To be opened by
G. B. Eusterman, Mayo Clinic, Rochester, Minn.

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MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Rothschild Amphitheatre, 2816 Ellis Avenue

(Capacity—330)

*Heart Study Group*

F-2a *A. Recent Studies of Coronary Diseases*

9:00– 9:10 Anatomical Observations.
Otto Saphir.
9:10– 9:20 Mechanism of Pain Production.
Louis N. Katz.
9:20– 9:30 The Electrocardiographic Diagnosis.
L. N. Katz, A. Bohning and H. Landt.
9:30– 9:40 Clinical Observations.
Walter W. Hamburger.

F-2b *B. The Thyroid and Heart Disease*

9:50–10:00 Heart in Hyperthyroid Disease.
William Buchbinder.
10:00–10:10 Masked Hyperthyroidism.
Morris W. Lev.
10:10–10:20 Dynamics of Heart Failure.
Louis N. Katz.
10:20–11:00 Total Ablation of the Thyroid as a Treatment of Congestive Heart Failure and of Angina Pectoris.
H. Blumgart, Beth Israel Hospital and Harvard University, Boston, Mass.

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F-3 MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Classroom of the Nurses' Home, 2816 Ellis Avenue

(Capacity—60)

11:00–12:00 Uses and Limitations of Encephalography.
A. Levinson.

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G MUNICIPAL TUBERCULOSIS SANITARIUM
(5601 N. Crawford Avenue, at Bryn Mawr Avenue)

Morgue, in the Laboratory Building

(Capacity—50)

10:00–12:00 Pathological-Clinical Conference.
Autopsy demonstrations.

Demonstration of specimens in museum.
Slide specimens and gross pathology.
Antemortem and postmortem x-ray plate demonstrations, in connection with pathological specimens shown.
Henry C. Sweany.

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H-1 NORTHWESTERN UNIVERSITY MEDICAL SCHOOL
(303 East Chicago Avenue)

Room 541

(Capacity—125)

9:10– 9:40 Orthopedic and Medical Management of Chronic Infectious Arthritis: Demonstration of Patients.
Emil Hauser.

9:40–10:10 (*a*) Cases of Chronic Infectious Arthritis Treated by Hyperpyrexia: A Review of Results.
(*b*) Knee-joint Visualization: Its Value in the Differential Diagnosis of Conditions Simulating Arthritis.
David E. Markson.

10:10–10:40 Medical Management of Chronic Obstructive Peptic Ulcer with Presentation of Cases.
Lowell D. Snorf.

10:40–11:10 Bronchiectasis: Demonstration of Cases.
Jerome R. Head.

11:10–11:30 Amebiasis.
A. A. Goldsmith.

11:30–12:00 Laboratory Diagnosis of Entameba Histolytica, with Microscopic Moving Picture.
Fred O. Tonney.

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H-2 NORTHWESTERN UNIVERSITY MEDICAL SCHOOL
(303 East Chicago Avenue)

Room 393

(Capacity—20)

10:00–11:00 Physical Therapy in Arthritis: Demonstration of a Program for Home and Office Treatment.
John S. Coulter.

11:00–12:00 Demonstration of Capillary Changes Following Physiotherapeutic Measures.
Gilbert H. Marquardt.

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H-3 PASSAVANT MEMORIAL HOSPITAL
(303 East Superior Street)

Room 108

(Capacity—25)

10:30–12:00 Oxygen Therapy: Demonstration of Oxygen Chamber, Tent and Catheter Technic.
M. H. Barker.

I-1 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

North Amphitheatre

(Capacity—75)

9:00– 9:30 Rôle of the Kidney in the Acid Base Balance of the Body.
Howard M. Sheaff.
9:30–10:30 Present Concepts of Bright's Disease.
Wilber E. Post.
10:30–11:30 Abdominal Enlargements in Children with Special Reference to the Spleen and Liver.
Clifford G. Grulee.
11:30–12:00 Behavior Clinic.
Harry R. Hoffman.

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I-2 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

South Amphitheatre

(Capacity—100)

9:30–10:00 Some Features of the Diagnosis of Amebic Dysentery.
Alva A. Knight.
10:00–11:00 Diarrheas.
Donald P. Abbott.
11:00–11:30 Toxic Effects from Alkalies in Ulcer Management.
L. C. Gatewood.
11:30–12:00 Pituitary Basophilism.
A. R. Colwell.

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J ST. LUKE'S HOSPITAL
(1437 South Michigan Avenue)

Nurses' Hall—2d Floor

(Capacity—250)

9:00– 9:30 Chronic Rheumatism of the Spine.
Joseph L. Miller.
9:30–10:30 (*a*) Surgical Treatment of Pulmonary Tuberculosis.
(*b*) Treatment of Bronchiectasis.
(*c*) Pulmonary Abscess.
Carl A. Hedblom.
10:30–11:00 Studies of the Peripheral Circulation.
Carl Johnson and George Scupham.
11:00–12:00 The Value of Malaria Therapy in Asymptomatic Neurosyphilis.
Paul O'Leary, Rochester, Minn.

Wednesday, April 18, 1934

A-1 UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Room P 117

(Capacity—256)

9:00– 9:30 A Case of Thickened Pericardium with Partial Pericardiectomy and the Clinical Syndrome of Portal Obstruction.
Louis Leiter and Dallas B. Phemister.

9:30–10:00 The Case Against the Nitrites in Angina Pectoris.
Emmet B. Bay.

10:00–10:45 Pain in Heart Disease.
Joseph A. Capps.

10:45–11:00 Heart Disease in Pregnancy.
Knute A. Reuterskiold.

11:00–12:00 Clinic on Heart Disease.
Alfred Stengel, Philadelphia, Pa.

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A-2 UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Room M 137

(Capacity—85)

9:00– 9:30 Clinic on Allergy.
Harry L. Huber.

9:30–10:00 Vasomotor Rhinitis.
Theodore E. Walsh.

10:00–10:30 Significance of Abnormal Variations in Acid-Base Balance.
A. B. Hastings.

10:30–11:00 A Discussion of Renal Function.
Henry L. Schmitz.

11:00–11:30 Renal Function Tests in Pregnancy.
William J. Dieckmann.

11:30–11:50 The Acid-Base Balance in Fatigue.
Frederic W. Schlutz.

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A-3 UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Outside of Room P 118

(No Set Capacity)

9:00–12:00 The Rôle of X-Ray in the Clinical Study of Heart Disease: Exhibition of Films.
Paul C. Hodges.

B

CHILDREN'S MEMORIAL HOSPITAL
(700 Fullerton Avenue)

Auditorium Nurses' Home

(Capacity—250)

9:00–10:00 Blood Disorders in Children.
Mila Pierce.
10:00–11:00 Cardiac Disease in Childhood.
Stanley Gibson.
11:00–12:00 Nephritis in Children.
C. A. Aldrich.

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C-1

COOK COUNTY GRADUATE SCHOOL OF MEDICINE
(In affiliation with the Cook County Hospital)
COOK COUNTY HOSPITAL
(West Harrison and South Wood Streets)

Medical Amphitheatre

(Capacity—150)

9:00– 9:45 Primary Carcinoma of the Lung, Clinical and X-Ray.
Aaron Arkin.
9:45–10:30 Chronic Lead Intoxication.
George W. Scupham.
10:30–11:15 Pericarditis.
Isadore N. Trace.
11:15–12:00 Verodigen (Digitalis) in Treatment of Heart Disease.
Italo F. Volini.

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C-2

COOK COUNTY GRADUATE SCHOOL OF MEDICINE
COOK COUNTY HOSPITAL
(West Harrison and South Wood Streets)

Surgical Amphitheatre

(Capacity—150)

9:00– 9:45 Pneumothorax.
Jacob J. Mendelsohn.
9:45–10:30 Polycythemia Vera: Chronic Hemolytic Icterus.
LeRoy H. Sloan.
10:30–11:15 Asthma and Asthmatoid Conditions.
Samuel M. Feinberg.
11:15–12:00 Chronic Arthritis: Bacteriologic Aspects.
Eugene F. Traut.

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C-3

COOK COUNTY GRADUATE SCHOOL OF MEDICINE
COOK COUNTY HOSPITAL
(West Harrison and South Wood Streets)

Amphitheatre, Children's Building

(Capacity—100)

9:00– 9:45 Endocrine Disturbances in Children.
Charles Stulik.

9:45–10:30 Nephritis.
Joseph K. Calvin.
10:30–11:15 Surgical Treatment of Tuberculosis in Childhood.
Joseph Greengard.
11:15–12:00 The Care of the Newly Born.
Craig Butler.

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C-4 COOK COUNTY GRADUATE SCHOOL OF MEDICINE
COOK COUNTY HOSPITAL
(West Harrison and South Wood Streets)

Bedside Clinics

(Capacity—15)

C-4a 9:00–12:00 Ward 65.
Aaron Arkin.
C-4b 9:00–12:00 Ward 64.
William J. Quigley.
C-4c 9:30–12:00 Ward 35.
George W. Scupham.
C-4d 10:00–12:00 Ward 45.
Samuel M. Feinberg.
C-4e 10:00–12:00 Ward 25.
Laurence E. Hines.
C-4f 10:00–12:00 Ward 63.
Sidney A. Portis.
C-4g 10:00–12:00 Ward 63.
Isadore N. Trace.
C-4h 10:00–12:00 Ward 60.
Leon Unger.
C-4i 11:00–12:00 Ward 15.
Clarence J. McMullen.
C-4j 11:00–12:00 Ward 61.
Frederick Tice.

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D UNIVERSITY OF ILLINOIS
(1817 W. Polk Street)

Room 106

(Capacity—200)

Frederick H. Falls and H. Douglas Singer Presiding

9:00– 9:20 The Use of Immune Serum in Puerperal Sepsis.
Abraham F. Lash.
9:20– 9:40 The Treatment of Menstrual Disorders by the Injection of Extracts of Anterior Pituitary Hormone.
William H. Browne.
9:40–10:00 Studies in Obesity with Presentation of Cases.
Robert W. Keeton.
10:00–10:20 Eclamptogenic Toxemia.
Frederick H. Falls.
10:20–10:40 The Tonic Pupil.
George B. Hassin.

10:40–11:00 Tumors of the Cord.
Eric Oldberg.
11:00–11:20 Psychiatry in General Practice.
H. Douglas Singer.
11:20–11:40 Contributions of the Oculist to Neurological Diagnosis.
Hallard Beard.
11:40–12:00 Speech after Laryngectomy with Case Demonstration.
Francis L. Lederer.

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E

LOYOLA UNIVERSITY and MERCY HOSPITAL
(2537 Prairie Avenue)

Amphitheatre

(Capacity—350)

9:00–10:00 General Medicine.
Walter G. McGuire.
10:00–11:00 Clinical Interpretation of Pain and Tenderness in the Abdominal Wall.
Peter T. Bohan, Kansas City, Mo.
11:00–12:00 Cardiac Clinic.
Robert S. Berghoff.

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F-1

MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Sarah Morris Amphitheatre, 2901 Ellis Avenue

(Capacity—170)

*Metabolism and Endocrine Glands*

9:00– 9:15 Influencing Metabolism by Surgical Methods.
L. Zimmerman.
9:20– 9:35 The Functions of the Hypophysis.
W. Saphir.
9:40– 9:55 Nephrosis.
Joseph K. Calvin.
10:00–10:15 Cholesterol Metabolism.
A. Mirsky.
10:20–10:35 Carbohydrate Disturbance in Hyperthyroidism.
S. Soskin.
10:40–11:00 Obesity.
Solomon Strouse.

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F-2

MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Rothschild Amphitheatre, 2816 Ellis Avenue

(Capacity—330)

*Tumor Clinic*

9:00– 9:45 Indications, Limitations and Advances in the Radium Treatment of Cancer. Lantern Slide Demonstration and Presentation of Treated Cases.
Max Cutler.

9:45–10:05 Immunological Phases of Experimental Carcinoma.
Bernard Portis.
10:05–10:25 Studies in Cancer Immunity.
W. Saphir.
10:25–10:40 Lymphoblastoma: An Analysis of 130 Cases.
L. M. Rosenthal.

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F-3 MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Main Building, Fifth Floor

(Capacity—20)

11:00–12:00 Ward Rounds.
Sidney Strauss.

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F-4 MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Classroom of the Nurses' Home, 2816 Ellis Avenue

(Capacity—60)

11:00–12:00 Injuries to the Vertebrae and Intervertebral Discs Following Lumbar Puncture.
C. N. Pease.

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G MUNICIPAL TUBERCULOSIS SANITARIUM
(5601 N. Crawford Avenue, at Bryn Mawr Avenue)

Amphitheatre, Fourth Floor, Middle Wing

(Capacity—60)

10:00–12:00 Diagnosis and Treatment of Pulmonary Tuberculosis.
Frederick Tice, Allan J. Hruby and Karl Henrichsen.

This clinic will afford opportunity for informal round table discussion of the new cases in the Receiving Ward of the institution; for the indication for treatment to be followed in the institution proper, with roentgenographic demonstrations.

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H-1 NORTHWESTERN UNIVERSITY MEDICAL SCHOOL
(303 East Chicago Avenue)

Room 541

(Capacity—125)

9:15– 9:40 Diffuse Osteoporosis Chiefly Involving the Spine: Etiology and Treatment: Case Reports.
Walter H. Nadler.
9:40–10:00 Hemolytic Icterus.
William H. Holmes.
10:00–10:30 Early Symptoms and Findings of Heart Failure in Hypertension: Demonstration of Patients.
M. H. Barker.

10:30–11:00 The Importance of the Diuretic Management of Congestive Heart Failure: Demonstration of Patients.
Paul Starr.
11:00–12:00 Heart Clinic.
James G. Carr.

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H-2 NORTHWESTERN UNIVERSITY MEDICAL SCHOOL
(303 East Chicago Avenue)

Room 267

(Capacity—25)

10:30–12:00 Clinic on Allergic Diseases: Demonstration of Patients and Diagnostic Procedures.
Samuel M. Feinberg.

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H-3 PASSAVANT MEMORIAL HOSPITAL
(303 East Superior Street)

Room 218

(Capacity—20)

11:00–12:00 Roentgen Demonstration of Interesting Gastro-Enterologic Cases.
James T. Case.

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I-1 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

North Amphitheatre

(Capacity—75)

9:00–10:00 Penetrating Crater Ulcers of the Duodenum.
Ralph C. Brown.
10:00–10:30 Esophageal Obstructions.
James B. Eyerly.
10:30–11:00 Pyloric Stenosis in Infancy.
Arthur H. Parmelee.

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I-2 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

South Amphitheatre

(Capacity—100)

9:00–10:00 Emergency Management in Ketogenic Acidosis Complicating Diabetes Mellitus.
Leo K. Campbell.

10:00–11:00 Non-Surgical Relief of Bladder Neck Obstructions with a Review of 400 Cases.
H. L. Kretschmer.

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I-3 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

"F" Operating Room, Presbyterian Hospital

(Capacity—20)

9:30–10:30 Vaginal Hysterectomy.
N. Sproat Heaney.

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I-4 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

Room 401, Rush Medical College

(Capacity—20)

9:30–10:00 Change in Thyrotoxic Heart Following Operation.
Charles Bacon.

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I-5 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

Library—Presbyterian Hospital

(Capacity—20)

11:00–12:00 X-Ray Conference.
C. B. Rose and F. Squire.

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J ST. LUKE'S HOSPITAL
(1437 South Michigan Avenue)

Nurses' Hall—2d Floor

(Capacity—250)

9:00– 9:45 Recent Advances in the Diagnosis and Treatment of Peripheral Vascular Disease.
Louis G. Hermann, Cincinnati, Ohio.

9:45–10:30 (*a*) Vascular Crises in High Blood Pressure.
(*b*) Hemorrhagic Nephritis.
(*c*) Heart Block and High Blood Pressure.
Arthur R. Elliott.

10:30–11:30 Effect of Splanchnic Section on Juvenile Diabetes.
Geza deTakats and George K. Fenn.

11:30–12:00 Roentgenograms of Tumors of the Bones.
E. L. Jenkinson.

K-1 VETERANS ADMINISTRATION FACILITY
(Hines, Illinois)

Amphitheatre

(Capacity—50)

9:30–10:15 Coronary Occlusion.
E. W. Hollingsworth.
10:15–11:00 Blood Dyscrasias.
E. W. Torrey.

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K-2 VETERANS ADMINISTRATION FACILITY
(Hines, Illinois)

Wards

(Capacity—20)

11:00–12:00 Ward Rounds.

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Thursday, April 19, 1934

A-1 UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Room P 117

(Capacity—256)

9:00– 9:45 Studies on the Nature and Inheritability of Cancer.
Maude Slye.
9:45–10:15 Bronchogenic Carcinoma.
Byron Francis.
10:15–10:45 Management of Carcinoma of the Esophagus.
Alexander Brunschwig and S. P. Perry.
10:45–11:15 Non-Specific Ulcerative Colitis.
Theodore E. Heinz.
11:15–11:45 Amebiasis and Amebic Dysentery.
Walter L. Palmer.
11:45–12:15 Motion Pictures of Gastrointestinal Motility.
A. J. Carlson.

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A-2 UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Room M 137

(Capacity—85)

10:00–10:30 Two Cases of Rat-Bite Fever with Unusual Mode of Transmission.
Herbert S. Ripley.
10:30–10:45 The Pathogenesis of Diabetic Vulval Pruritus.
H. C. Hesseltine.
10:45–11:15 Chronic Neutropenia.
L. T. Coggeshall.
11:15–12:00 Clinic on Diseases of the Blood.
O. H. Perry Pepper, Philadelphia, Pa.

A-3 UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Outside of Room P 118

(No Set Capacity)

9:00–12:00 The Rôle of X-Ray in the Clinical Study of Heart Disease: Exhibition of Films.
Paul C. Hodges.

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A-4 UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Room P 212

(Capacity—50)

*Demonstrations*

10:00–11:00 Blood Dyscrasias: Microscopic Demonstration.
E. Kandel.
11:00–11:30 The Outpatient Management of Diabetes.
Florence S. Smith (Introduced by Henry L. Schmitz).
11:30–11:45 The Fundus Oculi in Relation to General Medicine.
John T. Stough.
11:45–12:00 An Apparatus for Continuous Intravenous Injections.
Henry R. Jacobs.

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B CHILDREN'S MEMORIAL HOSPITAL
(700 Fullerton Avenue)

Auditorium, Nurses' Home

(Capacity—250)

*Surgical Disorders of Interest to the Internist*

9:00–10:00 Urology.
Herman L. Kretschmer.
10:00–11:00 General Surgery.
Albert H. Montgomery.
11:00–12:00 Orthopedics.
Fremont A. Chandler.

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C-1 COOK COUNTY GRADUATE SCHOOL OF MEDICINE
(In affiliation with the Cook County Hospital)
COOK COUNTY HOSPITAL
(West Harrison and South Wood Streets)

Medical Amphitheatre

(Capacity—150)

9:00– 9:45 Differential Diagnosis.
Frederick Tice.

9:45–10:30 Diabetes.
Clarence J. McMullen.
10:30–11:15 Some Aspects of Allergy.
Leon Unger.
11:15–12:00 Cardiac Pain.
Don C. Sutton.

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C-2 COOK COUNTY GRADUATE SCHOOL OF MEDICINE
COOK COUNTY HOSPITAL
(West Harrison and South Wood Streets)

Surgical Amphitheatre

(Capacity—150)

9:00– 9:45 Pulmonary Diseases.
Isadore A. Rabens.
9:45–10:30 Diseases of the Chest.
Ellis B. Freilich.
10:30–11:15 Pulmonary Diseases.
Samuel J. Taub.
11:15–12:00 Pneumoconiosis and Tuberculosis.
S. A. Levinson.

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C-3 COOK COUNTY GRADUATE SCHOOL OF MEDICINE
COOK COUNTY HOSPITAL
(West Harrison and South Wood Streets)

Amphitheatre, Children's Building

(Capacity—100)

9:00– 9:45 Diagnostic Value of Spinal Fluid.
Abraham Levinson.
9:45–10:30 The Problem of the Premature.
Julius H. Hess.
10:30–11:15 Treatment of Congenital Syphilis.
Samuel J. Hoffman.
11:15–12:00 Acute Otitis Media in Childhood.
Alfred Lewy.

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C-4 COOK COUNTY GRADUATE SCHOOL OF MEDICINE
COOK COUNTY HOSPITAL
(West Harrison and South Wood Streets)

Bedside Clinics

(Capacity—15)

C-4a 9:00–11:00 Ward 65.
Eugene F. Traut.
C-4b 10:30–12:00 Ward 64.
Italo F. Volini.
C-4c 11:00–12:00 Ward 61.
Frederick Tice.
C-4d 11:00–12:00 Ward 64.
LeRoy H. Sloan.

D

## UNIVERSITY OF ILLINOIS
(1817 W. Polk Street)

Room 106

(Capacity—200)

Carl A. Hedblom Presiding

9:00–9:20 Primary Carcinoma of the Lung, a Clinical and Pathological Report of 75 Cases.
S. A. Levinson.

9:20–9:40 Lung Tumors from the Radiological Viewpoint.
Adolph Hartung.

9:40–10:00 Indications for and Results of Therapeutic Pneumothorax.
Benjamin Goldberg.

10:00–10:20 Surgical Aspects and Demonstration of Cases.
Carl A. Hedblom.

10:20–10:40 Thromboangiitis Obliterans and Arteriosclerosis.
George Milles.

10:40–11:00 Methods of Evaluating the Element of Vasomotor Spasm in Thromboangiitis Obliterans.
W. J. Gillesby.

11:00–11:20 Cervicodorsal and Lumbar Sympathectomy in the Treatment of Thromboangiitis Obliterans and Raynaud's Disease.
Carl A. Hedblom.

11:20–11:40 Diagnosis and Treatment of Bronchiectasis: Case Demonstrations.
I. D. Thrasher.

11:40–12:00 Moving picture films showing end results.

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E

## LOYOLA UNIVERSITY and MERCY HOSPITAL
(2537 Prairie Avenue)

Amphitheatre

(Capacity—350)

9:00–10:00 Endocrine Clinic.
A. W. Schram.

10:00–11:00 Gastrointestinal Clinic.
Fred M. Drennan.

11:00–12:00 Cardiorenal Clinic.
Milton Mandel.

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F-1

## MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Sarah Morris Amphitheatre, 2901 Ellis Avenue

(Capacity—170)

*Heart Study Group*

*Recent Studies of Cardiovascular Disease*

9:00– 9:15 Chorea.
Jesse R. Gerstley.

9:15– 9:30 Convalescent Care of Cardiac Children.
Philip Rosenblum.

9:30– 9:40 The Relation of Subacute Bacterial Endocarditis to Rheumatic Endocarditis.
S. Wile and Otto Saphir.

9:40– 9:50 Treatment of Subacute Bacterial Endocarditis.
Walter W. Hamburger.

10:00–10:20 Peripheral Vascular Disorders.
S. Perlow.

10:25–10:35 A Method of Obtaining Heart Size Roentgenographically in Bedridden Patients at Ordinary Target Distance.
J. Brams, W. Brams and R. Arens.

10:40–10:55 Recent Observations on the Genesis of the Electrocardiogram.
L. N. Katz.

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F-2 MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Rothschild Amphitheatre, 2816 Ellis Avenue

(Capacity—330)

*Peptic Ulcer*

9:00– 9:20 Pathology.
Otto Saphir.

9:20– 9:40 Physiology.
H. Necheles.

9:40–10:00 Medical.
Jacob Meyer.

10:00–10:20 Surgical.
A. A. Strauss.

10:20–10:40 Roentgenology.
Robert Arens.

10:40–11:00 Discussion: To be opened by
Walter Alvarez, Mayo Clinic, Rochester, Minn.

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F-3 MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Ward of Main Building, Fifth Floor

(Capacity—20)

11:00–12:00 Correlation of the Eye Findings in General Medical Conditions.
L. L. Mayer.

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F-4 MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Classroom of the Nurses' Home, 2816 Ellis Avenue

(Capacity—60)

11:00–12:00 Perirenal Infections.
H. C. Rolnick.

G MUNICIPAL TUBERCULOSIS SANITARIUM
(5601 N. Crawford Avenue, at Bryn Mawr Avenue)

Surgical Amphitheatre, Fourth Floor, Middle Wing

(Capacity—50)

9:00–12:00 Surgical Clinic.
Richard Davison.

This clinic will afford opportunity to observe the treatment of tuberculosis by surgical methods, such as thoracoplasty, phrenico-exeresis, intra- and extrapleural pneumolysis.

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H-1 NORTHWESTERN UNIVERSITY MEDICAL SCHOOL
(303 East Chicago Avenue)

Institute of Neurology—Room 541

(Capacity—125)

9:15– 9:45 Diagnostic Significance of Pupillary Changes: Demonstration of Cases.
Lewis J. Pollock.

9:45–10:00 The Pathway for the Pupillary Light Reflex.
S. W. Ranson.

10:00–10:20 Some Aspects of Epilepsy.
Harry A. Paskind.

10:20–10:40 Blood Bromide Control of Epilepsy.
Benjamin Boshes.

10:40–11:00 The Influence of Hyperthyroidism on the Phospholipids of the Brain.
Arthur Weil.

11:00–12:00 Clinical and Experimental Relation of Pituitary, Hypothalamus and Sugar Metabolism.
David Cleveland and Loyal Davis.

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H-2 NORTHWESTERN UNIVERSITY MEDICAL SCHOOL
(303 East Chicago Avenue)

Room 393

(Capacity—20)

10:00–11:00 Physical Therapy in Arthritis: Demonstration of a Program for Home and Office Treatment.
John S. Coulter.

11:00–12:00 Demonstration of Capillary Changes Following Physiotherapeutic Measures.
Gilbert H. Marquardt.

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H-3 PASSAVANT MEMORIAL HOSPITAL
(303 East Superior Street)

No Program on Thursday

I-1 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

North Amphitheatre

(Capacity—75)

9:00– 9:30 Present Status of Coronary Thrombosis.
James B. Herrick.
9:30–10:00 Certain Features of Treatment of Cardiac Failure.
Fred M. Smith, Iowa City, Iowa.
10:00–10:15 Value of Serial Electrocardiograms in Coronary Thrombosis.
H. A. Richter.
10:15–11:00 A Moving Picture Showing the Relation of the Cardiac Cycle to the Electrocardiogram.
Clayton J. Lundy.

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I-2 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

South Amphitheatre

(Capacity—100)

9:00–10:30 Thyroid Clinic.
W. O. Thompson.
James H. Means, Boston, Mass.
10:30–11:00 Cryptogenic Fever in Ichthyosis.
Rollin T. Woodyatt.

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I-3 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

Room 302

(Capacity—20)

10:00–10:30 Cardiac Disease in Pediatric Practice.
Charles K. Stulik.
10:30–11:00 Migraine.
Peter Bassoe.

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I-4 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

Library, Presbyterian Hospital

(Capacity—20)

11:00–12:00 Pathology Conference Demonstrating Some Recent Concepts of Nephritis and Cirrhosis.
Carl W. Apfelbach.

J

ST. LUKE'S HOSPITAL
(1437 South Michigan Avenue)

Nurses' Hall—2d Floor

(Capacity—250)

9:00– 9:45 Congenital Heart Disease.
Louis F. Bishop, Jr., New York, N. Y.

9:45–10:30 Presentation of Brain Tumors with Roentgenograms.
Eric Oldberg.

10:30–11:15 The Importance of Cranial Roentgenograms in Neurosurgical Problems.
W. McKendree Craig, Rochester, Minn.

11:15–12:00 The Anemias.
John H. Musser, New Orleans, La.

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Friday, April 20, 1934

A-1

UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Room P 117

(Capacity—256)

9:00– 9:30 Hormones and Mammary Glands.
Carl R. Moore.

9:30–10:00 Recent Studies on the Male Hormone.
Fred C. Koch.

10:00–10:30 Indications of Hormonal Influences, other than Insulin, on Carbohydrate Metabolism.
B. O. Barnes.

10:30–11:00 Demonstration of Clinical Endocrinopathies.
Allen T. Kenyon.

11:00–12:00 Clinic on Thyroid Disease.
James H. Means, Boston, Mass.

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A-2

UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Room M 137

(Capacity—85)

9:00– 9:30 The Etiology of Gallstones.
Edmund Andrews.

9:30–10:15 Calcium Salts in Gallstones.
Dallas B. Phemister.

10:15–10:45 The Etiology of Non-Obstructive Jaundice.
E. S. Guzman Barron.

10:45–11:15 Toxic Hepatitis Due to Cinchophen.
Henry T. Ricketts.

11:15–12:00 Glycogen Storage Disease.
E. M. Humphreys.

A-3 UNIVERSITY OF CHICAGO—ALBERT MERRITT BILLINGS HOSPITAL
(950 E. 59th Street)

Outside of Room P 118

(No Set Capacity)

9:00–12:00 The Rôle of X-Ray in the Clinical Study of Heart Disease: Exhibition of Films.
Paul C. Hodges.

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B CHILDREN'S MEMORIAL HOSPITAL
(700 Fullerton Avenue)

Auditorium, Nurses' Home

(Capacity—250)

9:00–10:00 Present Status of Prophylaxis of Contagious Diseases.
Silber A. Peacock.
10:00–11:00 Behavior Problems in Children.
Bert I. Beverly.
11:00–12:00 Speech Defects in Children.
Frances Perlowski.

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C-1 COOK COUNTY GRADUATE SCHOOL OF MEDICINE
(In affiliation with the Cook County Hospital)
COOK COUNTY HOSPITAL
(West Harrison and South Wood Streets)

Medical Amphitheatre

(Capacity—150)

9:00– 9:45 Differential Diagnosis of Abdominal Pain.
Lee C. Gatewood.
9:45–10:30 Auricular Fibrillation.
Chauncey C. Maher.
10:30–11:15 Amebic Dysentery.
Alexander A. Goldsmith.
11:15–12:00 Pathology of Primary Carcinoma of Lung.
R. H. Jaffé.

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C-2 COOK COUNTY GRADUATE SCHOOL OF MEDICINE
COOK COUNTY HOSPITAL
(West Harrison and South Wood Streets)

Surgical Amphitheatre

(Capacity—150)

9:00– 9:45 Pulmonary Tuberculosis.
N. I. Fox.
9:45–10:30 X-Ray Studies in Pulmonary Tuberculosis.
Harry H. Freilich.

10:30–11:15 Diagnosis of Pulmonary Tuberculosis.
Harry S. Arkin.

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C-3 COOK COUNTY GRADUATE SCHOOL OF MEDICINE
COOK COUNTY HOSPITAL
(West Harrison and South Wood Streets)

Amphitheatre, Children's Building

(Capacity—100)

9:00– 9:45 Diagnosis of Syphilis in the Newly Born.
Arthur H. Parmelee.
9:45–10:30 Physical Examination of Younger Children.
Henry E. Irish.
10:30–11:15 Convalescent Serum in the Treatment of Contagious Disease.
Archibald Hoyne.
11:15–12:00 Urinary Retention in Childhood.
Patrick H. McNulty.

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C-4 COOK COUNTY GRADUATE SCHOOL OF MEDICINE
COOK COUNTY HOSPITAL
(West Harrison and South Wood Streets)

Bedside Clinics

(Capacity—15)

C-4a 9:00–11:00 Ward 61.
Lee C. Gatewood.
C-4b 10:00–12:00 Ward 45.
Samuel M. Feinberg.
C-4c 10:00–12:00 Ward 63.
Sidney A. Portis.
C-4d 10:00–12:00 Ward 60.
Leon Unger.

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D UNIVERSITY OF ILLINOIS
(1817 W. Polk Street)

Room 106

(Capacity—200)

Hugh A. McGuigan and William F. Petersen Presiding
9:00– 9:20 The Effect of Air Filtration on Seasonal Hay Fever and Pollen Asthma.
Tell Nelson and W. H. Welker.
9:20– 9:40 The Effect of Viosterol of High Potency on Seasonal Hay Fever and Asthma.
Ben Z. Rappaport.
9:40–10:00 Calcium Metabolism in Relation to High Viosterol Dosages.
C. I. Reed.
10:00–10:20 Effect of Ultraviolet Light on Sympatheticomimetic Drugs.
Hugh A. McGuigan and P. L. Ewing.
10:20–10:40 Hyperparathyroidism.
Lindon Seed.

10:40–11:00 A Cephalometric, Radiographic, Histologic Analysis of Dental Conditions in a Hypopituitary Case.
I. Schour and A. J. Brodie.
11:00–11:20 Creatine Metabolism in Childhood.
H. G. Poncher.
11:20–11:40 The Association of Meteorological Conditions and Diseases in General.
William F. Petersen.

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E LOYOLA UNIVERSITY and MERCY HOSPITAL
(2537 Prairie Avenue)

Amphitheatre

(Capacity—350)

9:00–10:00 General Medicine.
Walter G. McGuire.
10:00–11:00 Clinico-Pathological Conference.
E. L. Benjamin.
11:00–12:00 Cardiac Clinic.
Robert S. Berghoff.

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F-1 MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Sarah Morris Amphitheatre, 2901 Ellis Avenue

(Capacity—170)

*Diseases of the Chest and Infectious Diseases*

9:00– 9:20 Indications for Compression Therapy in Pulmonary Tuberculosis.
M. Biesenthal.
9:20– 9:40 Results Following Compression Therapy in Pulmonary Tuberculosis, X-Ray Case Demonstration and Follow-Up Statistics: Resumé of Work of Last Eight Years.
R. Bettman.
9:40–10:00 Studies on the Effects of Breathing Oxygen and Carbon Dioxide Enriched Atmospheres.
D. J. Cohn.
10:00–10:20 Results of Convalescent Serum Therapy during Past Three Years.
S. O. Levinson.
10:20–10:40 The Treatment of Empyema Thoracis; Explanation of the Rationale of the Closed Method of Drainage: Moving Picture Demonstration.
R. Bettman.

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F-2 MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Rothschild Amphitheatre, 2816 Ellis Avenue

(Capacity—330)

*Metabolism Group. Diabetes Mellitus*

9:00– 9:25 Newer Trends in the Treatment of Diabetes Mellitus.
Solomon Strouse.

9:30– 9:50 The Eye in Diabetes Mellitus.
H. Gradle.
9:55–10:20 The Metabolic Disturbance in Diabetes.
S. Soskin.
10:25–10:40 The "Diabetogenic" Hormone.
L. B. Shpiner.
10:45–11:00 Feeding the Diabetic Patient in an Outpatient Clinic.
Sarah Elkin.

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F-3 MICHAEL REESE HOSPITAL
(29th Street and Ellis Avenue)

Sarah Morris Hospital, 1st Floor, 2901 Ellis Avenue

(Capacity—60)

*Stomach Group*

9:00– 9:10 A Preliminary Report on the Secretion and Motility of the Stomach after Subtotal Gastrectomy.
Sigfried Strauss, A. A. Strauss, L. Scheman and H. Necheles.
9:10– 9:20 The Treatment of Peptic Ulcer with Powdered Okra.
Jacob Meyer and H. Necheles.
9:20– 9:30 Peptic Ulcer and Diabetes—Renal Glycosuria.
H. Binswanger and Jacob Meyer.
9:30– 9:50 Ulcerative Colitis; a Symposium: Medical and Surgical Aspects.
A. A. Strauss and Jacob Meyer.
9:50– 9:55 Duodenal Carcinoma; Report of Four Cases: Demonstrations of Specimens.
D. Rosenberg and Jacob Meyer.
9:55–10:10 The Effects of Peppermint Oil on Gastric Secretion and Motility.
Jacob Meyer, L. Scheman and H. Necheles.
10:10–10:25 The Effect of Peppermint Oil on Gastric Motility.
H. Sapoznik, R. Arens, H. Necheles and Jacob Meyer.
10:25–10:30 Teaching the Gastrointestinal Patient How to Eat.
Sarah Elkin and Jacob Meyer.
10:30–10:35 The Management of the Stomach Clinic.
Jacob Meyer and A. A. Strauss.
10:35–10:50 Chronic Jaundice.
A. A. Strauss.

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G-1 MUNICIPAL TUBERCULOSIS SANITARIUM
(5601 N. Crawford Avenue, at Bryn Mawr Avenue)

Amphitheatre, Fourth Floor, Middle Wing

(Capacity—60)

10:00–12:00 Clinical Conference on the Surgical Treatment of Tuberculosis.
Richard Davison, Karl Henrichsen and Frank Fremmel.

This clinic will afford an informal round table discussion of cases that have been treated with the various forms of collapse therapy, with demonstration of the cases and roentgenograms.

G-2 MUNICIPAL TUBERCULOSIS SANITARIUM
(2049 Washington Boulevard)

(Capacity—6)

10:00–12:00 An Extramural Pneumothorax Clinic.
Minas Joannides, Edmund L. Quinn, Emil Bunta and Clara Jacobson.

This clinic will afford opportunity to observe the actual technical work in pneumothorax therapy.

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H-1 NORTHWESTERN UNIVERSITY MEDICAL SCHOOL
(303 East Chicago Avenue)

Room 541

(Capacity—125)

9:15– 9:40 The Use of Chondroitin in the Treatment of Migraine, with Demonstration of Patients.
L. A. Crandall.

9:40– 9:55 Blood Changes Following Gastrectomy in the Rat.
Frederick Jung.

9:55–10:20 Experimental Studies on the Etiology of Anemia in Man and in Animals.
A. C. Ivy.

10:20–10:50 Treatment of Deficiency Anemias: Presentation of Patients.
Howard Alt.

10:50–11:20 A Report on the Percentage of Recurrences of Peptic Ulcer under Mucin Management, with Demonstration of Patients.
Samuel J. Fogelson.

11:20–12:00 Experimental Studies on the Value of Mucin in Peptic Ulcer.
A. C. Ivy, G. B. Fauley, John Orndoff and P. E. Reid.

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H-2 NORTHWESTERN UNIVERSITY MEDICAL SCHOOL
(303 East Chicago Avenue)

Room 267

(Capacity—25)

10:30–12:00 Clinic on Allergic Diseases: Demonstration of Patients and Diagnostic Procedures.
Samuel M. Feinberg.

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H-3 PASSAVANT MEMORIAL HOSPITAL
(303 East Superior Street)

Room 108

(Capacity—20)

10:30–12:00 Oxygen Therapy: Demonstration of Oxygen Chamber, Tent and Catheter Technic.
M. H. Barker.

H-4 PASSAVANT MEMORIAL HOSPITAL
(303 East Superior Street)

Room 218

(Capacity—25)

11:00–12:00 Roentgen Demonstration of Interesting Gastro-Enterologic Cases.
James T. Case.

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I-1 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

North Amphitheatre

(Capacity—75)

9:00– 9:45 Recent Concepts of Arthritis.
Ernest E. Irons.
9:45–10:30 Chronic Arthritis with Special Reference to Treatment.
Russell L. Cecil, New York, N. Y.
10:30–11:15 Liver Function Tests.
William J. Kerr, San Francisco, Calif.
11:15–12:00 Familial Icterus.
Evans W. Pernokis.

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I-2 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

South Amphitheatre

(Capacity—100)

9:00–10:00 Chronic Subdural Hematomas.
A. Verbrugghen.
10:00–11:00 Cardiac Arrhythmias.
Frank B. Kelly.
11:00–12:00 Renal Damage in Prostatic Obstruction Due to Bladder Compensation.
Robert H. Herbst.

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I-3 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

Room 302

(Capacity—20)

10:00–11:15 Modern Treatment of Pseudohypertrophic Muscular Dystrophy.
Richard B. Richter.
11:15–12:00 Lead Poisoning.
William D. McNally.

1-4 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

Room 401

(Capacity—20)

10:00–11:00 Surgery of the Thyroid Gland.
Edwin M. Miller.
11:00–11:30 Liver Treatment in Agranulocytosis.
R. W. Trimmer, H. M. Sheaff and F. L. Foran.
11:30–12:00 Neurological Clinic.
James C. Gill.

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1-5 RUSH MEDICAL COLLEGE and THE PRESBYTERIAN HOSPITAL
(1753 West Congress Street)

Library, Presbyterian Hospital

(No Capacity Indicated)

11:15–12:00 The Use of High Protein in Reducing Diets.
Anna E. Boller.

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J ST. LUKE'S HOSPITAL
(1437 South Michigan Avenue)

Nurses' Hall—2d Floor

(Capacity—250)

9:00–10:30 General Medical Clinic—"Weekly Grand Rounds."
Staff of St. Luke's Hospital.
10:30–11:00 Treatment of Angina Pectoris.
N. C. Gilbert.
11:00–12:00 Pathological Demonstrations.
Edwin F. Hirsch.

# COLLEGE NEWS NOTES

## Gifts Acknowledged

The following members have donated publications of which they are the authors, as indicated below, to the Library of the College. It is intended that this Library be a memorial to our members and consist principally of books of which members of the College are authors or joint authors.

Dr. J. Arnold Bargen (Fellow), Rochester, Minn.—1 book, "The Colon, Rectum and Anus";

Dr. I. M. Rabinowitch (Fellow), Montreal, Que.—1 book, "Diabetes Mellitus, A Handbook of Simplified Methods of Diagnosis and Treatment";

Dr. Joseph Hajek (Associate), New York, N. Y.—1 reprint;

Dr. James H. Hutton (Associate), Chicago, Ill.—6 reprints;

Dr. David E. Markson (Fellow), Chicago, Ill.—1 reprint;

Dr. Philip B. Matz (Fellow), Washington, D. C.—1 report on the residual effects of warfare gases;

Dr. Lewis J. Moorman (Fellow), Oklahoma City, Okla.—14 reprints.

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## New Life Members

Dr. Samuel E. Thompson (Fellow), Kerrville, Texas, and Dr. Philip H. Jones (Fellow), New Orleans, La., have become Life Members of the American College of Physicians, having contributed the prescribed life membership fee in accordance with the new plan of life membership recently adopted.

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Dr. John Dudley Dunham (Fellow), for many years Governor of the College for the State of Ohio, was recently chosen chief of the general staff of the Grant Hospital, Columbus. Dr. Dunham is also medical consultant for the Franklin County Tuberculosis Sanitarium and a member of the staffs of the Mt. Carmel and White Cross Hospitals.

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Dr. George R. Minot (Fellow), Boston, Mass., Professor of Medicine, Harvard University, delivered the twelfth lecture of the eighth series of afternoon lectures sponsored by The New York Academy of Medicine, on January 26. Dr. Minot's subject was "The Anemias—Etiology and Treatment."

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Dr. Donald Gregg (Fellow), Wellesley, Mass., is President of the Massachusetts Society for Mental Hygiene.

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Dr. J. Stuart McQuiston (Associate), formerly located in Rochester, Minn., removed on February 1, 1934, to 317 Higley Bldg., Cedar Rapids, Iowa, where he is engaged in private practice.

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Dr. Mark S. Knapp (Fellow), Flint, Mich., has retired from private practice and is devoting his entire time as Director of Medical Research of the Horace H. and Mary A. Rackham Fund.

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Dr. Samuel Weiss (Fellow), New York, N. Y., has been appointed Editor of *The Review of Gastroenterology*, the official organ of the Society for the Advance-

ment of Gastroenterology. This journal made its initial appearance February 15, as a quarterly journal devoted to gastroenterology, proctology and allied subjects.

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The Wyatt Research Foundation has been incorporated in the State of Arizona, "to conduct scientific investigations relative to the treatment and prevention of disease (particularly the arthritides) and the advancement of clinical and scientific medicine." The incorporators named are: Dr. Bernard L. Wyatt (Fellow), Laura W. Wyatt and Thelma G. Ream.

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Dr. S. A. Slater (Fellow), Worthington, Minn., presided as President over the Thirty-Ninth Annual Session of the Sioux Valley Medical Association at Sioux City, Iowa, January 23–24.

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At the last annual business meeting of the Institute of Medicine of Chicago, Dr. Joseph L. Miller (Fellow) was elected President and Dr. John Favill (Fellow), Treasurer.

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Dr. John E. Gordon (Fellow), Detroit, Mich., will be in charge of the new department of Epidemiology of the W. K. Kellogg Foundation. The department was established for the purpose of research in the control of communicable disease.

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Dr. Lewellys F. Barker (Fellow), Baltimore, Md., was elected a Vice-President of the Association for Research in Nervous and Mental Disease, at its last annual meeting in New York City.

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Dr. Bailey K. Ashford (Fellow), San Juan, Puerto Rico, recently retired as a colonel of the Medical Corps, U. S. Army, has been honored by the unanimous vote of the legislature of Puerto Rico in recognition of his being the founder of the School of Tropical Medicine and the initiator of the first campaign against hookworm disease in America. A bronze bust of Dr. Ashford will be placed in the government building in San Juan.

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Dr. Edward B. Vedder (Fellow), Washington, D. C., is President-Elect of the American Society of Tropical Medicine.

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Dr. Mills Sturtevant (Fellow) was recently appointed Professor of Clinical Medicine at New York University, and Dr. Warren Coleman (Fellow) was made Professor Emeritus of Clinical Medicine.

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Dr. Hugh Rodman Leavell (Fellow) has been appointed Health Commissioner of Louisville, Ky.

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Dr. Raphael Isaacs (Fellow), Ann Arbor, Mich., Dr. John A. E. Eyster (Fellow), Madison, Wis., and Dr. Andrew C. Ivy (Fellow), Chicago, Ill., delivered lectures in connection with a series of graduate lectures in physiology at Marquette University Medical School, sponsored by the educational committee of the Medical Society of Milwaukee County, during February and March.

Dr. George E. Pfahler (Fellow), Philadelphia, Pa., appears on the program of the fourth International Congress of Radiology, to be held in Zurich, July 24–31.

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The College of Physicians of Philadelphia and the American Academy of Political and Social Science held a joint meeting, February 7, for the discussion of "The Medical Profession and the Public: Currents and Countercurrents." Dr. Nathan B. Van Etten (Fellow), New York, spoke on "Abuses of Medical Charity and of the Free Services of Physicians." Dr. Roger I. Lee (Fellow), Boston, spoke on "The General Practitioner: His Place in the Medical Profession."

## *OBITUARIES*

### DR. JULIAN TURNBULL McCLYMONDS

Dr. Julian Turnbull McClymonds died December 4, 1933, in Berkeley, California. Dr. McClymonds was born in Winchester, Kentucky, November 26, 1870. He received his pre-medical training at the University of Kentucky and his M.D. from the University of Michigan Medical School, 1894; he did postgraduate work at the University of Vienna, University of Paris and Mt. Vernon Hospital. The greater part of his professional life was spent in Lexington, Kentucky, where he was a member of the Lexington Clinic from 1920 to 1931. He was First Assistant Surgeon, University of Michigan Medical School, 1894–1895; First Assistant in Hygiene and Physiological Chemistry at the same school, 1896–1898; Consulting Physician Good Samaritan and St. Joseph's Hospitals, Lexington, Kentucky, 1912–1931; assisted in organizing Hospital Unit No. 40, "The Barrow Unit," for service in the World War, and during his service in this country and in France, he was promoted from the rank of Lieutenant to that of Lieutenant Colonel, being retired from active service at the close of the war and commissioned a Colonel of Reserves, U. S. Army Medical Corps. He was a member of his County and State societies, a Fellow of the American Medical Association, Southern Medical Association and a Fellow of the American College of Physicians since 1920. He retired from practice in Lexington and went to Berkeley, California, where his death occurred as a result of heart disease.

ERNEST B. BRADLEY, M.D., F.A.C.P.,
Governor for Kentucky.

### DR. GEORGE HUNTER

Dr. George Hunter (Fellow), died on December 12, 1933. Dr. Hunter was born in Illinois. He early came to California. He was graduated from the College of the University of California, at Berkeley, in 1903. In 1906 he received the degree of Doctor of Medicine from the same institution. In 1907 he came to Los Angeles and began the practice of medicine.

Dr. Hunter was an outstanding member of both the Los Angeles County Medical Association and the California State Association, having held offices and sat in the Councils of both of these organizations. He held many positions of honor and trust in the medical societies to which he belonged. He was a Past President of the Los Angeles County Medical Association, of the Clinical and Pathological Society, and of the Society for Psychiatry and Neurology. He was a member of the Board of Councilors of the California Medical Association, a Fellow of the American College of Physicians, a member of the Psychopathic Association of California, and a member of the Insanity Commission of the State. He was a member of the Staff of the Los Angeles General Hospital for twenty years and served on the Staffs of St. Vincent's, the Cedars of Lebanon, California and the Santa Fe Hospitals. During the War, Dr. Hunter was a Captain in the Medical Corps with Base Hospital Number 35 in France. In addition to these activities and the crowded days of a busy life he found time for special study periods in the neurologic centers of Philadelphia, Boston and Baltimore.

The Associations to which Dr. Hunter belonged and scientific medicine, especially in the fields of neurology and psychiatry, have sustained a great loss in his death. The community in which he lived will miss an earnest medical practitioner and civic worker. Dr. Hunter had a most pleasing personality. His attachments were full and deep. He was a friendly man and his friendship was given without reservations. His death came as a shock to the members of the profession and the citizens of the community in which he lived. The memory of the man and of the good he did will long be with us.

EGERTON CRISPIN, M.D., F.A.C.P.,
Governor for Southern California.

## DR. ARTHUR D. DUNN

Dr. Arthur D. Dunn (Fellow), Omaha, Nebraska, died January 8, 1934, from a heart affection; aged sixty-six years.

Dr. Dunn was a native of Meadville, Pa. He held the degree of Bachelor of Arts from Allegheny College, 1896; Doctor of Philosophy from the University of Chicago, and Doctor of Medicine from Rush Medical College, 1892. He was house physician at Cook County Hospital and a private assistant to Dr. John B. Murphy. He went to Omaha in 1907, and is said to have been the earliest exponent of real scientific medicine in the Missouri Valley. He was coroner's physician in Omaha for one and one-half years, exerting great influence in the introduction of the value of autopsies to members of the profession of Omaha. Dr. Dunn was professor of medicine at Creighton University College of Medicine from 1908 to 1922; a member of the Advisory Board and vice-dean of the same institution from 1914 to 1922; professor of experimental medicine and chairman

of the Department of Clinical Research at Nebraska University College of Medicine from 1924 to the time of his death.

He was a member of the Nebraska State Medical Association and served as its delegate to the American Medical Association several years. He was a Fellow of the American Medical Association and served on its Council on Medical Education a number of years. He was also a member of the Central Society for Clinical Research, past president of the Missouri Valley Medical Society, and president-elect of the Omaha-Mid-West Clinical Society. He was elected a Fellow of the American College of Physicians in 1918, and served for several years as the Governor of the College for Nebraska.

Dr. Dunn was the author of numerous scientific articles appearing in leading medical journals, and was much in demand as a speaker at medical meetings, locally and nationally.

ADOLPH SACHS, M.D., F.A.C.P.,
Governor for Nebraska.